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THE TREATMENT OF OBESITY

A Review of the Literature and a Follow-up Study of Fasted Patients

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INTRODUCTION

Obesity remains a medical enigma (1). Defying clear definition as a clinical entity, a myriad of therapeutic approaches to obesity have been attempted over the years with a remarkably consistent low degree of success (2, 3). The approaches have been diverse - medical, surgical, psychiatric, social - and reflect the complexity of the problem of the obese state. Recently an apparent increase in interest has arisen in the treatment of obesity, as reflected in the medical literature. This has likely been catalyzed by the relatively recent growing enthusiasm and concomitant growing fear and skepticism over newer methods of treatment: intestinal bypass surgery and behavior modification. A careful re-evaluation of the treatments of choice for the obese patient is needed at this time. In addition to an examination and comparison of results of various

treatment methods, it is important to reconsider the basic understanding of obesity in order to rationally approach the problem therapeutically. Epidemiologic and etiologic considerations should not be forgotten, lest our means may obscure our goals.

The potpourri of treatment approaches may be indicative of the confusion and misunderstanding rampant among physicians concerning obesity. However, an eclectic approach could be the result of good clinical judgement in individualizing treatment for a very complex problem. More disturbing than the variety of therapeutic approaches is the relative lack of any approach. Obesity is often not defined as a clinical problem and, for a variety of reasons is too often ignored by the physician in the clinical setting. Perhaps the greatest deterrent is the fact that obesity is so difficult to treat successfully. This is undoubtedly discouraging, but clearly not the only factor, as physicians treat many disorders despite very limited success. Underlying the problem of the treatment of obesity is the realization that obesity, unlike most other clinical disorders, is to a great extent a moral issue (4). Obesity is often simplified into issues of will power and gluttony - morally-charged items - and the burden and responsibility of care is frequently thrust back upon the shoulders of the obese patient. Although some advantage may be achieved through bolstering the patient's motivation and

also limit-setting his dependency needs, the moralistic approach has serious drawbacks. It often reflects a physician's ignorance about the obese state, and in its insensitivity to the patient may be a disservice. Again, a more rational approach to the obese patient can be found after understanding the basics of the clinical disorder and reviewing the results of different therapeutic approaches.

One difficulty in the study of obesity results from the incremental nature of this disorder rather than it being an all-or-none pathologic entity. Clinically, however, obese patients may present with seemingly different medical problems. Commonly seen is the mild or moderately obese patient whose obesity is incidental or at most questionably associated with other health problems for which he seeks relief. Here, obesity is usually looked upon as a symptom (5) and may or may not be viewed as an important problem requiring treatment. The massively obese patient, on the other hand, perhaps presenting with a Pickwickian syndrome, severe hypertension or other serious problems felt to be directly related to a more obvious life threatening obesity, is usually approached more aggressively for the treatment of his major disorder of obesity. The medical literature rarely makes a distinction between these two groups of obese patients. Such a distinction is increasingly needed in obesity research now that the more risky surgical approach is gaining acceptance. This study will review literature about obesity in general,

realizing that dividing obesity into quantified categories is often unnecessary and impractical. However, some attention will be focussed upon the problem of massive obesity and its treatment.

THE OBESE PATIENT

Definition

A dictionary defines obesity as "excessive fatness, corpulence, or overweight." (6).Jean Mayer stresses that obesity is a pathologic condition, characterized by an accumulation of fat much in excess of that necessary for optimal body function. (8).Salans similarly defines obesity as "a disorder in which there is an abnormal enlargement of the adipose tissue mass." (9).Mayer makes a distinction between obesity and overweight, the former meaning too much fat, the latter less specifically meaning too much weight. The heavily muscled and boned individual is likely to be found overweight, but may not be obese. Swings in water balance may also affect weight by up to several pounds. A theoretical distinction between obesity and overweight exists. Accepting the concept of

"too much fat," one must consider the limitations of normal body fat content. In men, normal body fat content increases with age from about 18-20% at age 20 to about 35% at age 60. For women the respective numbers are 20-25% and 25-30%. (10).Equating obesity with adiposity is limited by the validity of these ranges of normal values. Is an elderly thin man too fat because 30% of his weight is adipose tissue? It must also be kept in mind that normal ranges are usually defined by assuming a normal distribution and then choosing a somewhat arbitrary boundary such as that defined by the standard deviation from the mean, establishing the upper 16% of the sample as above normal. (8).The concept of normalcy is further obscured when considering obesity in terms of hypothalamic regulation. If an individual's hypothalamic regulatory system is set to maintain fat stores at a high level (11), then that person's obesity is a normal or ideal set point for his body composition (12).

Although George Bray defines obesity as an enlargement and/or hyperplasia of adipose cells, he stresses his conviction that obesity is a symptom rather than a disease. (21)"It represents one visible consequence of ingesting more calories than are being utilized" (5). He derives this notion from the apparent heterogeneity of the obese state. Hilda Bruch states that: "Obesity...must be looked upon as the outward manifestation of a variety of underlying disturbances in weight and appetite

regulation" (14). Even Mayer, who is convinced that a somatic regulator underlies the process, sees obesity as multicausal, a common symptom of numerous conditions, and therefore offering multiple cures.(4)

Measurement

Accepting that obesity is a symptom of diverse causes characterized by an overaccumulation of body fat, its clinical measurement and assessment is a problem. Indirect rigorous laboratory measurements offer the most scientifically sound method of estimating degree of adiposity. Densimetric, hydrometric (dilution), and body potassium determination methods have been developed (4), but are not practical for clinical use. Of anthropometric measures, that of skinfold thickness remains the best accepted. The validity of this measure is based upon the belief that subcutaneous fat, evenly distributed, is directly proportional to total body fat in an individual for a given age and sex. It requires the use of a special caliper and some minimal skill at least in measuring the thickness of a pinched skinfold, usually over the triceps. This measurement is compared with standardized tables. Although Mayer sees this method as simple, practical, and precise (15), its use in clinical settings has not been popular and it remains a diagnostic tool of the researcher and specialist.

Measurement of height and weight remains the most used method for determining obesity. Standard tables take into account height, body build, sex and age in setting limits for normal weight. The inadequacy of using weight to measure obesity has been mentioned, and can be both falsely high or low, as Keys found twenty per cent of underweight men in the upper one third of fatness distribution (16). The tables are derived from insurance company data (17) which has been criticized as of limited usefulness because of population skewing (18). To reduce inaccuracy introduced into normal range values by variations in non-adipose tissue contributing to weight, the height-weight tables show different normal weight ranges for small, medium and large frame. This variable relates to Sheldon's earlier work on somatotypes (19). Sheldon defined three basic genetic body types: endomorphic, mesomorphic, and ectomorphic, based upon seventeen anthropometric measurements. Not only do these variations in body build or type make obesity interpretation difficult, but the somatotype itself may be closely associated with a predisposition to obesity. Seltzer and Mayer found obesity to correlate with endomorphy in adolescent girls (20). In spite of the limitations of the standardized height-weight tables, Bray found a good correlation ($r=+0.9$) between table assessment of obesity and adiposity measured densimetrically (21). To reduce the overinfluence of height in the use of the tables and increase accuracy, the ratio of weight/height squared, called body mass index, was found to best correlate with adiposity (16).

Subjective assessment of fatness can in most instances be crudely accurate and may be helpful in detecting obese patients who are not overweight. The mirror test is practical, although often unreliable: if you look fat, you are.

TABLE 1
STATISTICAL BULLETIN METROPOLITAN LIFE INSURANCE COMPANY NO. 40
NOVEMBER-DECEMBER, 1959 DESIRABLE WEIGHTS IN INDOOR CLOTHING

Height	Weight (lb.)		
	Small frame	Medium frame	Large frame
5'2"	112-120	118-129	126-141
3"	115-123	121-133	129-144
4"	118-126	124-136	132-148
MEN 5"	121-129	127-139	135-152
6"	124-133	130-143	138-156
Aged 7"	128-137	134-147	142-161
25 8"	132-141	138-152	147-166
and 9"	136-145	142-156	151-169
over 10"	140-150	146-160	155-174
11"	144-154	150-165	159-179
6'0"	148-158	154-170	164-184
1"	152-162	156-175	168-189
2"	156-167	162-180	173-194
3"	160-171	167-185	178-199
4"	164-175	173-190	182-204

Height	Weight		
	Small frame	Medium frame	Large frame
4'10"	92-98	96-107	104-119
11"	94-101	98-110	106-122
5' 0"	96-104	103-113	109-125
WOMEN 1"	99-107	104-116	112-128
2"	102-110	107-119	115-131
Aged 3"	105-113	110-122	118-134
25 4"	108-116	113-126	121-138
and 5"	111-119	116-130	125-142
over 6"	114-123	120-135	129-146
7"	118-127	124-139	133-150
8"	122-131	128-143	137-154
9"	126-135	132-147	141-158
10"	130-140	136-151	145-163
11"	134-144	140-155	149-168
6" 0"	139-148	144-159	153-173

Prevalence

Not altogether independent from the determination of normal values for weight, skinfold, or indirectly measured adiposity, is the prevalence of obesity. On the height-weight tables (17) the upper limit of desirable weight is about five per cent above the mean of a given range for a height and frame. Desirability, in this case, has been based upon mortality data. The U.S. Society of Actuaries in 1960 found the following per cent deviation from desirable weight (17,22)

		% Of Population Weighing X% From Ideal Weight			
Age (Years), Sex		-10%	+10%	10-19%	+20%
20-29	♂	13	31	19	12
50-59	♂	4	63	29	34
50-59	♀	4	67	21	46

Although this very large study was limited to insured individuals, smaller studies in the U.S. and Great Britain have found between 18-34% of the adult population to be at least 10% overweight (23-25). In the New York City public school system, 10% of the children are overweight (26). 75% of obese children are believed to go on to become obese adults, while 25% of obese adults were obese children (27). A more recent Public Health Service report estimates that 25-45% of American adults are greater than 20% overweight (28). Generally, clinical obesity is considered significant when excess weight

is at 10-15%, and 20-30% overweight is excessive obesity (29).

Risks and Consequences

Although the prevalence of obesity is impressively large, the clinical significance of obesity lies in the associated risks, hazards, and liabilities that are caused by or related to the obese state. Two basic schools exist on the hazards of obesity. Mann has called obesity the "nutritional spook," (30) emphasizing that the evidence is weak correlating obesity with the disease states it is usually said to be associated with. Furthermore, Mann is impressed that "obesity is a relatively incurable disorder," (27) which would imply that the treatment may often be more drastic than the disease. The more traditional point of view stresses that obesity is a menace (31,4).

The hazards of obesity could be categorized as follows: 1- increased disease risk; 2- effect on established disease or normal function; 3- social and psychological effects; 4- costs and hazards of treatment. Mortality statistics for life insurance holders in the 1930's document, if only crudely, the considerably increased mortality risk for overweight persons (see table 2) (4). Overall, the mortality for the overweight population is 150% that of the normal. Furthermore, the mortality increases as the percentage of overweight increases.

TABLE 2
PRINCIPAL CAUSES OF DEATH AMONG MEN AND WOMEN RATED FOR OVERWEIGHT
ATTAINED AGES 25-74 YEARS

Ratio of Actual to Expected Deaths According to Estimates of Contemporaneous Mortality Experience on Standard Risks

Metropolitan Life Insurance Company, Ordinary Department
Issues of 1925 to 1934, Traced to Policy Anniversary, 1950

Cause of Death	MEN		WOMEN	
	Deaths	% Actual of expected Deaths	Deaths	% Actual of expected Deaths
Principal cardiovasc.-renal diseases	1867	149	1103	177
Organic heart dis., coronary artery dis.	1377	142	697	175
Cerebral hemorrhage	247	159	226	162
Chronic nephritis	243	191	180	212
Cancer, all forms	385	97	476	100
Stomach	62	85	34	86
Liver and gall bladder	33	168	46	211
Pancreas	19	93	21	149
Breast	--	--	81	69
Uterus	--	--	103	121
Diabetes	205	383	235	372
Tuberculosis (all)	24	21	20	35
Pneumonia	98	102	78	129
Cirrhosis	96	249	32	147
Appendicitis	76	223	41	195
Hernia and intestinal obstruction	39	154*	31	141*
Gall bladder dis. (all)	32	152*	30	188*
Biliary calculi	19	206	50	284
Stomach and duoden. ulcer	30	67	--	--
Puerperal conditions	--	--	43	162
Suicide	63	78	23	73
Accidents, total	177	111	74	135
Auto	76	131	27	120
Falls	32	131	--	--

*Based on mortality rates on Standard risks for 1935-1939

NOTE: Percentages which have been underlined indicate statistically significant deviations from experience on Standard risks.

Serious lifeshortening diseases said to be associated with obesity include hypertension, diabetes mellitus, sudden death, hyperlipidemia, respiratory insufficiency, toxemia of pregnancy, thromboembolic disease, and congestive heart failure (31-33). Diseases of moderate to severe morbidity said to afflict the obese include gallstones, osteoarthritis, varices, hernias, menstrual disturbances, depression, anxiety and anesthetic risk (31, 34, 28). Minor disorders such as dermatitis, flat feet, impaired agility, and heat intolerance can impair life style and, as has been reported in obese children, can lead to serious accidents such as burns (35). Numerous other problems less often associated with obesity have been reported.

The Framingham Study found hypertension ten times as prevalent in those 20% or more overweight as compared to normal weight (36). Although other studies also show a significant association between overweight and high blood pressure (37, 38), the degree of obesity has not been well correlated with hypertension (39). In fact, the correlation between blood pressure and adiposity has been found to be of low order in several studies, between .05 and 0.3 (40,36). McDonough et. al. found a positive correlation in black women, but not black men in their study in Georgia (41). Body weight has been found to better correlate with hypertension than has body fat (36,42). The use of weight as a measure for obesity rather than indirect measures of adiposity allows for the influence of body build

per se to remain uncontrolled for in most studies. Mayer and Seltzer have found a positive correlation between mortality and body build (20, 4). Obese individuals are most often endomorphic in somatotype, and least often ectomorphic (4). The contribution of bone and muscle mass as compared to adipose tissue mass to increased mortality and morbidity in overweight individuals is not yet clear.

The increased mortality for overweight people from heart disease and especially coronary artery disease (see table 2) implies a strong association. The Framingham Study found a correlation for angina and for sudden death for those 20% or greater overweight (43). Keys also found a correlation, but this disappeared when he considered only normotensive overweight individuals (44). To add to the uncertainty, other studies have failed to show a significant correlation between overweight and coronary artery disease (45,46). As obesity appears to be associated with hypertension and hyperlipidemia (47, 48), and these conditions predipose to coronary artery disease (49), it is reasonable to infer that obesity is a potential culprit at least by association and possibly by cause in a subpopulation of obese patients that have abnormalties in their blood pressure and serum lipids. Furthermore, it appears that obese individuals who suffer myocardial infraction with or without their obesity playing an etiologic role are compromised in their ability to recover (43).

Whether this increased rate of sudden death in the obese is due to an increased hydraulic load upon the heart (39) or poor collateral circulation due to the relative inactivity associated with obesity (50), or a combination of these factors is not known.

The distinction between cause and association must be kept in mind in these considerations of the hazards of obesity. Associations between obesity and disease are often found, particularly with the use of retrospective studies. Disease caused by obesity is better assessed through prospective studies and requires difficult and sometimes unfeasible control of multiple variables. For example, if a prospective study shows a significant association between obesity and the onset of coronary artery disease, we do not know whether a cause and effect relationship exists or that some other factor such as decreased exercise (50-52) is primary to both conditions in these individuals.

The relationship between obesity and abnormal glucose tolerance and diabetes mellitus is less controversial. (See table 2). Here, the disease state is more clearly related to the physiological alterations which obesity causes in carbohydrate metabolism. The obese have been found to have increased fasting insulin levels, theorized as an adaptation from active obesity (state of accumulation of fat) for increased efficiency and rapidity in the removal of glucose from the blood (53). It appears that the obese often have a

decreased carbohydrate handling capacity, that they require more insulin to act upon adipose and muscle cells (exacerbated by an increased cortisol secretion), and that this is clinically reflected in an abnormal glucose tolerance test and sometimes leading to overt diabetes mellitus (54,17). In Sims' study on human hyperphagia, normal male volunteers were overfed to study the changes caused by exogenous obesity. In the group which successfully reached 20% overweight, a diminished glucose tolerance, increased insulin levels, and increased peripheral insulin resistance were found (55-57).

A major mechanism of disadvantage in obesity is that of mechanical burden; obese people overwork their systems. Although this is still somewhat controversial in the cardiovascular system, it is more obvious in the muscular-skeletal system. Arthritis, fractures, and other muscular-skeletal problems are often troubled by excess weight. Respiratory difficulty, manifested in extreme in the Pickwickian syndrome, is believed to be another mechanical consequence of obesity (49). When obesity is a mechanical burden to health, the degree of obesity would seem to correlate with the degree of disability.

Other mechanisms of disadvantage have been suggested. Hypothetically, the increased food intake of the obese introduces the increase of ingestion of noxious substances (27). Indeed, laboratory animals have been found to live longer on a diet restricted to three-quarters of their usual intake

as compared to a group on an ad libitum diet (58). Decreased physical activity might also play a role in disease predisposition in the obese. While a number of studies have shown an association between inactivity and obesity (50-51, 59-61), and some have implicated inactivity in an etiologic role (52), Sims' work on experimental human obesity suggests that inactivity can be secondary to the gain of excess weight (56).

The potential social and psychological consequences of obesity are mostly obvious and can be devastating. A long social history of prejudice against fat people exists. The obese are somehow viewed as physically and morally absurd. Anthropological precedents of obesity as an indicator of success still have some meaning in our culture, but the prestige accrued upon the "fat cat" or the "buddha" in certain settings is more than offset by the negative aspects of being considered physically and often morally grotesque. Mayer is struck by the social attitudinal aspect of obesity (4), and it may indeed be this quality of obesity, rather than a more "medical" one, that makes it such a difficult disorder to deal with successfully in a medical model.

Social ostracism and prejudice naturally relate to the psychological trauma of obesity. Although it is difficult to separate psychological problems that are causal from those consequential to obesity, disturbances in self-esteem, sexuality, and body image, as well as neurotic depression may be

manifested. Hilda Bruch emphasizes that obesity is associated with many psychological disorders, rather than just one. In obese children, their development centers around their fatness. While eating freely, they tend to avoid activities and contacts, not unlike the situation described for the symbiotic preschizophrenic family (14). A number of investigators have found evidence of greater psychopathology in obese versus nonobese patients on the basis of psychological testing or clinical evaluation (62, 63). These studies, however, do not determine whether the psychological disturbance is primary or secondary to the obesity. The psychological aspects etiologically related to obesity will be discussed in another section.

Not to be forgotten amongst the hazards of obesity are those resulting from weight reduction therapy. In addition to the side effects of drugs, fasting, intestinal bypass surgery (to be discussed when considering these treatments), abused methods, and folk remedies, even moderate dieting can produce untoward reactions. Stunkard has reviewed the literature linking diet with depression and concludes that untoward emotional reactions to diet are a real phenomenon especially in patients with juvenile onset obesity undergoing severe caloric restriction as outpatients (64). Bruch warns that:

> ...for many people overeating and being fat is a balancing factor in their adjustment to life. Ineffective as it is, it represents the best form of adaptation that such people have been able to make. (65)

Thus is the concept viewing obesity as a depressive equivalent for some individuals (66).

Other hazards have been reported. Mortality data indicate significantly raised death rates in overweight people for a number of surgical disorders such as appendicitis, hernia, gall bladder disease, and intestinal obstruction (17). Other relatively obvious risks exist, although seldom documented. For example, physical examination of the abdomen is often difficult in the obese patient and important physical findings are frequently not detected. Less obvious risks have also been reported, such as the association between nephrotic syndrome and massive obesity (67).

The purported benefits of obesity should be mentioned. Mortality data imply a significant decreased risk for breast cancer, tuberculosis, peptic ulcer, and suicide. It is unknown whether these benefits are truly obtained through adiposity or by some other variables common to the group of overweight patients. The theorized anti-depressant effect of obesity has been mentioned, and Simon found overweight Air Force men less depressed than their normal peers (66).

In sum, the hazards of obesity are numerous and diverse, including physical and psychological problems, from trivial to life threatening, and through a variety of pathogenetic mechanisms. Controversy arises concerning the degree that

obesity predisposes to hypertension and its related serious diseases of the cardiovascular-renal systems. Diseases more clearly related to physiological disturbances brought on by the obese state, such as diabetes mellitus, are more closely associated with obesity.

The benefit of weight reduction in terms of relieving the hazards of obesity is a major consideration for initiation of therapy. Marks found a return to normal mortality rates for a group that had successfully lost weight (37). This data, however, is crude and imperfect and a good study testing whether weight loss in obese subjects lowers their risk for certain diseases is relatively unfeasible. Mann asserts that weight reduction for hypertension is not reasonably worthwhile considering the infrequency of successful treatment (27).

An individualized risk-benefit analysis seems prudent in the decision to treat patients for obesity. The following salient points should be kept in mind:

1) Obesity carries with it numerous and various potential consequences to an individual's physical and emotional health.

2) Weight reduction will relieve or prevent these consequences to a varying and uncertain degree, depending largely upon the physiological relationship of adiposity or overweight to the consequence, and the reversibility of the consequence.

3) Weight reduction therapy is generally lengthy and costly,

accompanied by a variety of potential side effects, depending on the method, and, for the most part, is unsuccessful in the long run.

Therefore, no hard and fast rule can be applied to the question to treat or not to treat. Patient motivation is, of course, another important variable, and will be discussed when considering treatment efficacy.

Classification

The classification of obesity has undergone several revisions in its basic scheme this century. Van Noorden introduced the endogenous-exogenous classification at the turn of the century (5), and it is still often used today. Exogenous implies that the obesity is caused by overeating, while endogenous obesity implies some explainable physiologic or genetic mechanism. While of some practical use, such as differentiating between endocrine causes and so-called dietary causes, this classification falls short in its theoretical accuracy. There is formidable evidence, to be discussed shortly, that would lead us to believe that so-called exogenous obesity is no more exogenous or unphysiologic than the endogenous obesity seen in Cushing's syndrome. Clinical use of this categorization is further hampered by connotations that these labels have taken on over the years: exogenous obesity

as the result of an incorrigible and immoral gluttony versus the respectable and treatable disease-caused endogenous obesity.

A more recent development has been the so-called anatomic classification: hypertrophic versus hyperplastic obesity. A potentially important categorization arose on finding hyperplasia of adipocytes in juvenile onset obesity, and only hypertrophy without increased cellularity in the adipocytes of patients who first became obese in adulthood (72-75). The potential therapeutic relevance of these findings are felt in light of the understanding that weight reduction will decrease adipocyte size but not cell number (74, 76). Interest has been sparked in early life and the factors that increase cellularity. Knittle and Hirsch found they could modify cell number in young rats nutritionally, implicating the importance of overnutrition in early life in juvenile onset obesity (77).

A number of classification schemes based upon etiology or clinical types have been devised (4,5)(78,79). (See table 3). While Mayer limits his classification to genetic, hypothalamic, and endocrine categories (4), Bray adds to this group the categories of inactivity, drugs, and essential obesity (5). Within this classification, simple obesity, considered as a genetic obesity, is by far the most common, and the type that interests us the most.

TABLE 3
CLASSIFICATION OF OBESITY IN MAN: ETIOLOGIC
Modified from Bray (5)

Hypothalamic
  Tumors
    Solid (Fröhlich syndrome)
    Leukemia
  Inflammatory
  Traumatic
  Increased intracranial pressure
    Empty sella
    Pseudotumor cerebri

Endocrine
  Cushing's syndrome
  Insulinoma
  Castration
  Stein-Levinthal syndrome
  Pregnancy
  Hypothyroidism

?Inactivity

Genetic
  Simple; Juvenile onset
  Laurence-Moon-Biedl syndrome
  Hyperostosis frontalis interna
  Alstom's syndrome
  Prader-Willi syndrome

Drugs
  Phenothiazines
  Estrogens
  Cyproheptadine

Etiology

The understanding of the etiology of a disease is often the key to the development of an effective treatment. Obesity, hardly well conceptualized as a disease state, suffers the dilemma of etiological uncertainty, which has likely contributed to its relative refractoriness to a variety of imperfect

therapies. However, obesity is the result of any of a multiplicity of causes, and likely can be approached, theoretically at least, through a number of potential cures (4).

Mayer has stressed the importance of animal studies in understanding human obesity: "Is man indeed unique as far as normal - and pathological - fat accumulation is concerned?"(4) Animal husbandry is an example of genetics operating in obesity outside of the laboratory setting. A number of rodent models exist of genetically determined obesity (4,68). The yellow mouse transmits obesity by autosomal dominance, while several other mice strains show autosomal recessive transmission. Obesity is also observed in a number of inbred strains such as the New Zealand obese mouse and the Japanese K K mouse. Although these genetically determined obese animals have a number of characteristics in common, such as hyperphagia, inactivity, hyperglycemia, and hyperinsulinemia, no clear biochemical basis for explaining the obesity has been determined (5).

Human studies indicate that genetics plays a role in obesity. Newman found identical twins separated at birth to be significantly closer in weight than a group of fraternal twin controls (69). More recently Shields found separated monozygotic twins closer in weight than dizygotic twins reared together, implicating genetics as more influential than environment in body

weight (70). Work earlier this century showed stoutness to be transmitted as a Mendelian inherited dominant trait (71). Gurney found the following in the population he studied (39).

Parents	Stout Offspring
stout x stout	73%
stout x nonstout	40%
nonstout x nonstout	9%

Worth mention are a number of reported hereditary syndromes that include obesity in their constellation: Laurence-Moon-Biedl, hyperostosis frontalis interna, Alstrom's, and the Prader-Willi syndrome (5).

Although the evidence is strong that hereditary factors contribute to the emergence of the formerly labelled exogenous obesity (less controversially called simple obesity by Mayer (4)), it is less clear to what extent this is true. A multiplicity of genes is likely involved (4). Evidence suggest that hyperplastic obesity, the juvenile onset type, may be genetic.

Endocrine obesities, it should be stressed, are relatively rare as compared to simple obesity. Cushing's syndrome is perhaps best known, the hyperadrenocorticism producing a characteristic clinical and laboratory picture, including a truncal, posterior cervical, and superclavicular fat distribution. Hyperinsulinism is another endocrine abnormality that can

produce obesity (81). The pathophysiology of insulinomas is relatively clear, but the hyperinsulinism and associated weight gain frequently known to precede diabetes is less well understood in its relationship to obesity. Sims showed that hyperinsulinism and abnormal glucose tolerance could occur after a significant weight gain in overfed subjects (55), although evidence of these insulin changes preceding obesity in the prediabetic has not been established.

Of some appeal is the concept that obesity is the result of a hypometabolic state. The endocrinological prototype of this phenomenon is best seen in hypothyroidism. These patients have a decreased metabolic rate and tend to gain weight, although it is unclear how much of this weight gain is due to fat and how much is fluid. Hypothyroidism, however, needs be verified by thyroid function tests and not diagnosed solely on the basis of a basal metabolic rate (BMR) measurement, as has been done so often in the past. Although it is quite possible that the obese burn up less energy in their daily activities (82), BMR studies have mostly shown no difference from normals (29). Passmore found that obese patients gained more than thin patients when overfed for fourteen days (83,84). Such evidence that the obese are not as capable of burning up extra fuel may relate to Rolly's observation in 1921 that the thermal response to food is decreased in obesity (29). It is theorized by some that the thermal effect of eating - the specific dynamic

action of food - allows normal individuals to maintain weight with varying intakes. In Miller's thermogenesis theory the specific dynamic action decreases in obesity (85). Galton has postulated a possible enzyme deficiency based on his evidence that the obese have reduced ability to oxidize glyceral phosphate, leaving more glycerol available for fat syntheses(86).

These metabolic findings and theories are of yet unclear importance in the etiology of obesity. More likely may be their importance in the maintenance of the obese state. Craddock summarizes that the metabolic differences between the obese and normal are "...of degree only and are due to adaptation to an abnormal intake of food at some time." (29)

Other endocrinological diseases associated with obesity are a number of varying gonadal disorders. Male hypogonadism is often associated with a truncal obesity. Stein-Leventhal syndrome, or polycystic ovary disease, consists of hypo- or amenorrhea, often infertility, hirsutism, and sometimes obesity in young women. These women show increase adrenal and ovarian function, and a hyperphagia and weight gain that has suggested hypothalamic involvement in the process, although there is little data to support this (87). Hypothalamic lesions have also been suggested in Fröhlich's syndrome, inwhich truncal obesity is associated with sexual infantilism, and often other abnormalities. This syndrome may be associated with tumors and other disorders of the hypothalamic pituitary area and, like the rare hereditary Laurence-Moon-Biedl syndrome,

obesity and genital atrophy are assumed but as yet unproven to be the result of hypothalamic dysfunction.

Although of great importance theoretically, hypothalamic obesities are rare. Three pathologic groups exist: traumatic, inflammatory, and neoplastic. The most common cause has been the craniopharyngioma (5). Animal experiments have uncovered the physiology of the hypothalamic regulation of satiety and hunger. Destruction of the ventromedial area of the hypothalamus caused a number of different animals to overeat until obese. Destruction of lateral hypothalamic areas produced animals that would not eat. On the basis of these and other findings the mechanism for the regulation of food intake has been postulated: a satiety center in the ventromedial nucleus and a feeding center in the lateral hypothalamus, with connnections between the two centers (4, 49).

Subsequent theories have integrated the appetite centers into a scheme of abnormal regulation. "Glucostatic," "lipostatic" and "aminostatic" theories of food intake have emerged with the basic idea that some blood factor, falling below a critical level, stimulates hypothalamic centers through specific receptors, producing the drive to eat. Mayer's glucostatic theory has received widest interest (4, 29), postulating that hypothalamic glucoreceptors register low levels of effective blood glucose in some individuals causing them to eat more.

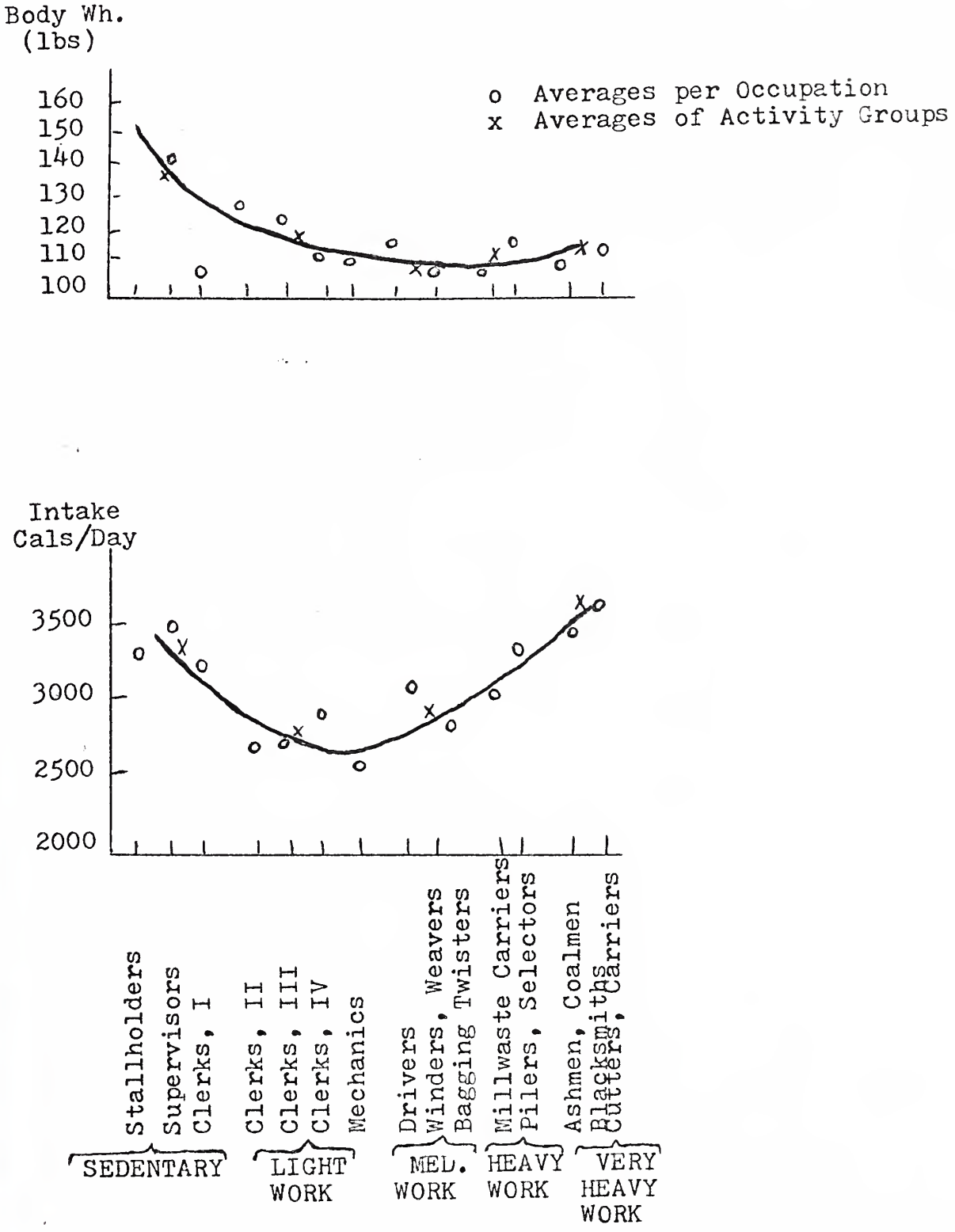
What has emerged has been the concept of obesity, in many if not most cases, as a disorder of hunger and satiety regulation. It seems likely that an individual, based upon his genetic predisposition and early nutritional experience, has his regulatory mechanism for food intake set at a certain level. For the obese, this level is set high. Indeed, there are many physiological and behavioral similarities between the obese man and the normal hungry person (12). Both obese and hungry subjects have been found to eat faster (88), to more readily eat in a new environment (12), and to prefer good over bad tasting food (33, 89) more so than normal controls. Schacter has conducted a number of studies of eating behavior that implicate poor regulation of intake or an insensitivity to physiological cues in the obese (88, 90). These behavioral eating patterns of obese and hungry subjects are similar to those found in animals with experimental ventromedial hypothalamic lesions. A physiological index of hungry, free fatty acid in blood, is found to be inflexibly elevated in obese subjects (91).

The clinical implications of this view of obesity are profound. If the obese patient "overeats" to meet the needs of a true physiologic hunger, how successful can he be in first losing weight and then maintaining his weight against a chronic hunger? Such a situation could help explain both the high failure rate for long term weight reduction and the phenomenon of dieting depression.

Another seemingly important factor in the unsimple etiology of simple obesity is that of inactivity. Basically, obesity is the result of a positive caloric balance: the energy absorbed is greater than the energy expended. This balance is exquisitely regulated in normal individuals who can generally eat as they please and maintain their weight, even though an imbalance of only one hundred calories per day could lead to an accumulation of ten pounds of fat over a year. Rats were found to maintain a stable weight on an ad libitum diet when they were exercised between one and five hours per day. Below one hour, however, the regulatory mechanism seemed to fail, and the rats gained weight (92). Mayer's study of Indian industrial workers showed a similar phenomenon. (See figure 1). Over a range of light work jobs through very heavy work jobs, workers maintained normal weights by natural variations in their caloric intake. However, workers in sedentary jobs weighed more than their active fellow workers and showed a caloric intake greater than others expending more energy (52). Other studies have linked obesity with inactivity, if not as a cause, then at least as a factor contributing to its maintenance. Chirico used pedometers (50) and Bullen used time lapse motion pictures (51) to show that obese subjects were less active than controls. Sims, who overfed normal volunteers, found his subjects more inactive when they became obese (55).

FIGURE 1

BODY WEIGHT AND CALORIC INTAKE AS
A FUNCTION OF PHYSICAL ACTIVITY IN MAN

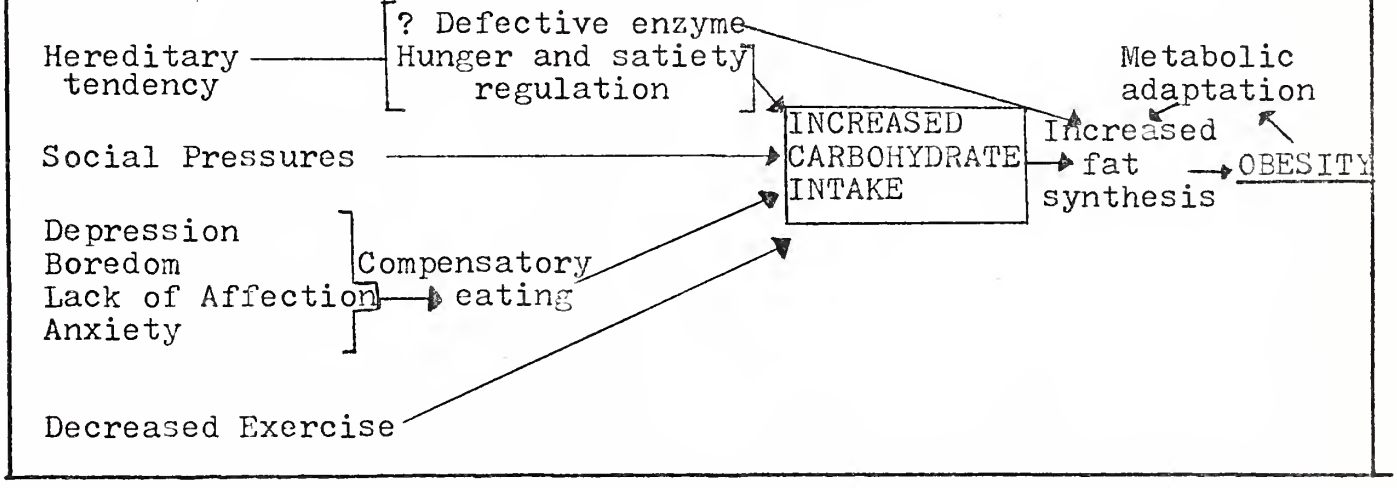


A behavior as complex as eating must include consideration of psychological factors in its etiology. In the 1940's many considered obesity as the expression of a neurosis (29). This simplistic view has fallen out of vogue in light of a more sophisticated neuro-humoral understanding of obesity. However, evidence still implicates the importance of psychological factors. A number of studies have found obese subjects to score more abnormally than controls on a variety of psychological tests (62,63,93). Bruch and Yudkin have articulated the concept of compensatory eating (65,94): a basic need to have a large body to compensate for inferiority feelings. Stressful or anxiety-provoking situations cause some obese individuals to eat more (95). Stunkard postulates that some obese have serious disturbances of body image (96). In this maze of theory we must respect Bruch's reminder that obesity is probably associated with a number of psychological disorders, not one, and her caveat that identifying psychological problems as a cause of obesity versus an effect of weight reduction is very difficult (14). Craddock's statement seems functional even if of unproven accuracy: "The majority of obese people probably have no obvious psychologic factors affecting their tendency to obesity" (29). Nevertheless, Bloom and Clarke's invention of the descriptive term "Obese Carboholic" (97) reflects the view that many clinicians take towards their obese patients: victims of a psychological addiction and physiologic craving for food.

Interacting with the psychological factors relevant to becoming obese are a number of social factors. The Mid-Manhattan Study found only 5% of upper class women overweight contrasted to 30% for the lower class (98). Social eating and exercise habits, education, ethnic and societal differences, and cultural sexual role differences can all affect one's tendency to become obese.

The inadequacy of classifying simple obesity as a genetic obesity is obvious after considering the complex metabolic, psychological, and social factors relevant. However, such a classification can be helpful in defining other obesities in which the etiology is better understood. Craddock's concept of the etiology of simple obesity well depicts the interplay of a variety of factors that may lead to obesity (29). (See Figure 2).

Figure 2
THE ETIOLOGY OF SIMPLE OBESITY
(Modified from Craddock (29))



Summary and Conclusions

The definition, measurement, prevalence, hazards, classification, and etiology of obesity have been reviewed and considered. Accepting the definition of excess adiposity, clinical measurement is practically limited to indirect measurement, height and weight tables being accurate for most cases, and skinfold thickness measured by caliper offering greater accuracy. Prevalence data indicate that obesity is very common, although reports vary. The hazards of obesity are numerous and varied, some obvious and others controversial, some trivial and others life-threatening. Weight reduction will clearly alleviate and prevent certain problems of the obese, but it is of uncertain benefit for other problems. Obesity has been classified and reclassified, based upon newer etiological understandings. Numerous disorders of both man and animal are associated with obesity, but these are relatively rare as compared to simple obesity. Recently divided into juvenile and adult onset types based upon anatomic differences of the adipose tissue, simple obesity appears to be influenced by genetic, metabolic and behavioral factors in its genesis and maintenance. Although several appealing theories exist, a clear etiologic understanding of obesity awaits further progress, and weight reduction therapy through establishing a negative caloric balance can be approached via a number of routes by which obesity is influenced.

TREATMENT

Introduction

The decision as to whether or not to treat an obese patient is a problem that has been discussed in the section considering the hazards of obesity and benefits of weight reduction. Worth reitering is the point that this is a dynamic decision for the physician and the patient in which many variables need be considered in a risk-benefit model. Mayer's contention that weight reduction is desirable for all obese patients (8) lacks realism, while Mann's view dubbing obesity as the "nutritional spook" (30) seems unduly conservative in its approach. More appropriately, no hard and fast rules need be made concerning indication and contraindiction as long as the patient's total well-being is of utmost priority.

A distinction ought to be made between patient education and actual patient treatment for obesity. The former includes disclosure to the patient that he is clinically overweight, that this condition is hazardous to his health, and that it is advisable for him to reduce his weight towards normal. This is clearly a service to most patients and will undoubtedly often result in some small degree of success, especially when the physician-patient relationship is particularly strong. However, a clear and well-thought out treatment plan is more appropriate if the physician seriously seeks a successful outcome for the patient. It has been shown that some fifty per cent of obese patients seen are not treated, even when greatly overweight (100).

The wide variety of treatments for obesity reflect both the multiplicity of etiologic avenues that have been theorized and the failure of any single method to be satisfactorily effective for most patients. However, a common denominator exists in all reasonable methods: a negative caloric balance must be achieved to lose weight, and over the long run, caloric balance must be equilibrated to avoid regaining the weight.

Feinstein has pointed out that although a plethora of methods exist, there is little scientific data to help the physician decide which is best. In evaluating methods, he offers several caveats: success should be based upon relative achievement of target weights; dropout need be considered; follow-up need be considered; guard against bias (101).

Several criteria have been devised to measure the success of weight reduction methods, such as rate of weight loss, amount of weight lost, or per cent of excess weight lost. These criteria, Feinstein has noted, are not valid in that they are too greatly affected by initial weight or early program dropouts. His reduction index relates loss to both initial weight and surplus weight, but without being influenced by duration (102).

> Reduction Index= % of weight loss x relative initial obesity = weight loss/weight surplus x initial weight/ target weight x 100

Feinstein considered an index of sixty as successful. Target weights can be determined from height/weight tables or based upon clinical judgment. Since its introduction some fifteen years ago the reduction index has seldom appeared in the literature and the degree of its use is unknown.

Diet

The diet has long been the mainstay of obesity therapy. Its appeal lies in that it is "natural", introduces a minimum of iatrogenic manipulation, is inexpensive, and is syntonic with the concept that obesity is an eating disorder. And, indeed, calories do count - a concept that appeals to the lay scientific mind of contemporary man. The basal metabolic rate for man calculates to about 1000 calories/square meter/day; the 5'10" 150 pound man having a surface of about 1.7 m^2.

Daily activity burns calories in excess to the BMR an average of sixty per cent for adolescents and some forty per cent for those over the age of sixty (103). However, energy expenditure can vary markedly, ranging between 2400 and 6000 calories/day for a male (4). A pound of fatty tissue contains about 3500 calories (104).

Despite these metabolic realities, dieting has been largely unsuccessful in the long term treatment of obesity. Stunkard reviewed literature reported over a ten year period, finding under twenty-five per cent of all patients undergoing treatment having lost up to twenty pounds, and about five per cent having lost as much as forty pounds (2). Finding only eight follow-up reports, he located only two out of one hundred patients who lost twenty or more pounds and who maintained their loss after two years. A number of other reports and estimates give these success rates for dieting regimens: ten-forty per cent of patients lose weight after one year; one to thirteen per cent maintain some loss after five years (23,29,101,105-109).

A wide variety of diets have been used to achieve an overall decrease in caloric intake. Simplest of these is the prescribed low caloric diet that is well-balanced - what might be called a "common sense" diet. Obviously, this common sense approach usually fails, or otherwise it would preclude the numerous other diets that have appeared. Significantly decreasing food intake is clearly difficult for most obese persons, explainable by some of the psychological and physiological factors mentioned.

Defaulting is a major impediment to success. Bulk agents, most notably methylcellulose, have been tried in the hope that satiety could be achieved through both psychologic and physiologic mechanisms of eating and filling the stomach with moderately large amounts of food. A large study found no benefit of use of bulk agents (110) and it is suggested that naturally bulky foods - fruits and vegetables - can serve as well (4). The use of artificial low carbohydrate foods and sweeteners is another attempt to lessen the burden of a decreased caloric intake. Used widely in a program in which calories are truly saved, these "diet foods" can be helpful, but their impact has been minimized because of unpalatability, expense, the low appeal of synthetic chemicals in food, and their use without a well-planned reduction program.

Because of the difficulty of compliance with the low caloric diet and its high failure rate, special diets have been devised that are less harsh in terms of decreased food but will purportedly reduce weight if adhered to because of manipulation of foodstuffs in the diet. The recommended balanced diet ought to contain a minimum of 14% protein, a maximum of 30% fat, and the remainder of calories as carbohydrate (4). Kekwick and Pawan postulated that a fat mobilizing substance produced after fat ingestion led to an increased weight loss in subjects on diets high in fat over subjects on other isocaloric diets (111-115). Pennington began using the "high fat" diet on his obese patients with some success about

twenty-five years ago (116), and the diet was subsequently modified by Donaldson who added large water intakes to the regimen (29). Yudkin found that strict carbohydrate control was all that was necessary for a successful diet, allowing his patients a free fat and protein intake (117). Although others have demonstrated the effectiveness of low carbohydrate/free fat and protein regimens (118, 97), Pilkington contends that the diet seems to work because of the high fluid retention of carbohydrates (119), while Young claims that evidence implies an increase in fat metabolism (120). Another metabolic mechanism that might favor a diet high in protein is the high specific dynamic action of this foodstuff which would theoretically dissipate some protein calories.

The major advantage of the free diet is clear: make it easy enough for the dieter to allow success. Craddock, an advocate of the free diet, writes:

> That the free diet is satisfactory for use in general practice is shown by the fact that almost every patient who takes his dieting seriously can lose weight for a month or two even if he has not the motivation to maintain dietary control for a longer period (29).

Such claims have been challenged, however, and a number of studies have found no benefit of special diets with a variety of foodstuff ratios over the balanced diet (121,122,129) Also, foods contain mixtures of fat, protein and carbohydrates and significantly altering the ratios of these foodstuffs from that of a normal diet is difficult to achieve. The benefit of the free diet is further obscured by the criticism that it is unsafe

nutritionally - particularly in promoting hyperlipidemia through a high fat intake - fails to guide the obese patient towards new healthier eating habits.

Another special diet devised to make compliance easier has been the formula diet. Here, the patient is permitted one or several prepared nutriment fluid meals per day and no other caloric food. It claimed the advantage of being simple, safe, and by offering the patient a rigid but simple regimen to follow was conducive to high compliance and success. Although early trials were promising (102), the formula diet faded quickly as a popular method.

Recently, Sohar carried out a follow-up study of 27 patients that had successfully dieted fourteen years previously. More than two-thirds of the group showed no substantial decrease from their pre-diet weight; only five had lost more than ten per cent of their weight, while three had gone on to gain more than ten per cent (123). Is dieting a worthwhile treatment? George Bray and George Mann, with long and scholarly interests in the field, think not (27,124). This view is derived with the following in mind: 1) dieting is often arduous and emotionally and physically upsetting; 2) it is an expense (professional care) and inconvenience; 3) it often fails to reduce weight short term, and usually fails long term; 4) (Mann) - weight reduction is often unnecessary for the well-being of the patient.

Why do diets usually fail? The concept that likens the obese person to a normal hungry person (12) (both neurohumorally

and behaviorally), discussed previously, allows us to understand how difficult it must be to voluntarily abstain from food in the face of a constant and powerful basic human drive: hunger. Psychological factors have also been mentioned, and the obese patients who use eating in response to or in relief of emotional stress (compensatory eating) (24) may find it extremely difficult to diet. Weight loss in the dieter can be described in two phases: an initial fluid loss, often an encouragaing start, then followed by a slower and more gradual loss that represents the catabolism of fat (125). This second stage can be frustrating to both patient and physician. As discussed earlier, the obese are highly efficient in utilizing calories, probably through metabolic adaptation (226, 83,84), and this is compounded by a tendency to adapt to caloric restriction by decreased energy expenditure (127). The result is a disappointing degree of weight loss that is less than the predicted amount even though the patient has adhered to the diet.

Another vital factor relevant to the success or failure of a diet is that of patient compliance. Feinstein found restricted environment programs - inpatient programs that assured the necessary discipline - superior to unrestricted environment programs, and found the degree of successful weight loss to be directly proportional to the amount of caloric restriction (102). Based upon his analysis of methods, Feinstein defined three inter-

actional factors that influence diet adherence:

1) Patient: variety of psychic factors; motivations

2) Patient-physician relationship: role of the doctor; number of visits; clinic availablility; incentives by physician; physician attitude

3) Diet program: factors which tend to keep patient on program - enthusiastic beginnings and novelties.

He concludes that the particular diet is least important in success, that the physician - patient relationship is most important, and that "when a patient is ready to diet, he can lose weight with whatever method of caloric restriction is given him."

The importance of motivation has also been noted by others. Craddock found that his obese patients with medical reasons for losing weight did twice as well as his other obese patients (29). Of note is that the best long term results of dieting for a large program were reported for the Anti-Coronary Club of New York - a group of highly motivated volunteers (109). The patient-physician relationship is of importance in any medical regimen that calls for voluntary patient compliance. Craddock emphasizes the need to individualize therapy as best suited to each patient. Besides taking a history and doing a physical examination, he administers a psychological test - the Shipman Anxiety/Depression Scale questionnaire(128) - to help determine neurotic tendencies that might alter treatment and prognosis. He stresses the importance of physician interest,

especially in terms of advising and educating the patient about a suitable program, and sees his patients every two weeks at first, and then monthly (29). As Hollenberg has stated:

> Successful management (of obesity) when it does occur, is the result of a knowledgeable and sympathetic physician having the time and the interest to meet repeatedly with a patient who has at least a modicum of insight into the condition and a considerable motivation to reverse it (29).

Exercise

The therapeutic partner to the diet is exercise. This is logical in light of our understanding that calories do count. The role of inactivity in the etiology of obesity has been discussed, as has been mentioned the wide range of caloric expenditure found in people with different activity levels. Exercise alone cannot be considered a reasonable weight reduction program. As Mayer has shown, increased energy expenditure is naturally offset by increased caloric intake in the nondieting individual (52). Increasing energy expenditure without a matching increase in intake can be an effective part of a weight reduction program. Energy expenditure is proportional to body weight for a given exercise, making this a self-correcting factor in the active person (4). A three mile walk in one hour burns only about three hundred calories, but Keys calculates that a 190 pound man walking an hour daily for three months will lose an additional ten pounds (129). (See Table 4)

TABLE 4

ADDITIONAL WEIGHT LOSS FROM EXERCISE
Modified from Keys and Craddock (29)

One hour's walking daily (or 3/4 hour's bicycling or 1/4 hour's swimming or 1/2 hour's tennis)

Weight lb.	One Month lb.	Two Months lb.	Three months lb.
130	2.2	4.4	6.5
145	2.5	4.9	7.3
160	2.8	5.5	8.1
175	3.1	6.0	8.9
190	3.4	6.5	9.6
225	3.9	7.7	11.3
250	4.3	8.6	12.7

Craddock concludes: "an increase in the amount of regular exercise taken should be part of the weight reduction regime for every patient with no medical contraindications: (29). However, the benefit of exercise may not be so predictable. Buskirke has shown that when obese patients increase their energy expenditure and restrict their intake, they compensate by conserving energy for the remainder of their nonstrenuous activities (130).

Little has been written about which individual factors are associated with a good or poor prognosis for successful treatment. Not surprising is the observation that obese adults who were obese as children are less likely to succeed in weight reduction and maintenance (109). The recent anatomic distinction between juvenile and adult onset obesity may help explain this,

but psychosocial factors are also likely to be contributory. Also well known is that massive obesity is a more difficult problem than obesity of a more moderate degree. Again, several factors could easily explain this. Craddock, who admittedly sees little massive obesity in his practice, has identified a number of prognostic factors in his obese patient population (29). He reports that his patients with high incomes did better. This is probably a cultural phenomenon, and class values and education may play a role as well as enhance physician-patient rapport. Craddock reports that patients with medical incentives to lose weight did twice as well as the other patients. The importance of motivation has been discussed earlier, and perhaps no motivation is as strong as a medical one. Of note is his observation that exercisers did better. Other favorable prognostic characteristics include male sex, married, and parents (29, 109, 242). Patients with a strong compulsion to eat do badly. Craddock concludes:

> The patient who has the best chance of dieting successfully...is a successful businessman or professional man who has become moderately obese during his adult life, is married with children, emotionally mature, and with no marked tendency to depression.
>
> His success will be quicker if he can take extra exercise and if he has a medical reason for losing weight. Unfortunately, less than 10% of the patients with a weight problem who present themselves to a physician come into this category.

Drugs

While diet and exercise have the appeal of simplicity, their

relative lack of success has led to a search for a medical treatment for obesity. Bray predicts that ultimately a successful treatment for moderate or severe obesity will be pharmacologic (131).

However, no drug thus far has shown outstanding effectiveness and drug treatment is considered an adjunct to a dietary program and not a reasonable treatment without dieting.

A great deal of experience exists with the use of appetite suppressing agents of the amphetamine type. These numerous agents, all bearing chemical resemblance to the parent compound D-amphetamine probably produce relative anorexia through stimulation of the ventromedial hypothalamic satiety center (4) or through another central nervous mechanism (132, 133), although peripheral metabolic process have also been suggested as contributing to their effectiveness (134). The effectiveness of these agents on weight reduction over placebo has been documented in numerous studies (135-140). Using well-controlled and double-blind methods (138), the literature supports the effectiveness of these agents even in the face of the difficulty of isolating drug effect from variables related to the dieting regimen. Also well documented is the limited duration of these drugs' effects (141). Most of the above studies documented positive results for twelve weeks or less, and four to six weeks may be the optimal period for most patients (4). One small study found an anorexiant (diethylproprion) to be inferior to placebo after

one year of use (142).

Another serious limitation to the usefulness of these agents is the associated side effects. Undesirable side effects resemble those found with use of the prototype drug, amphetamine: central nervous stimulation effects - restlessness, anxiety, insomnia, and similar symptoms manifested in extreme by psychosis; cardiovascular effects - including headache, palpitation and cardiac arrhythmias, angina, and other less common problems; excessive sweating; gastrointestinal effects-dry mouth, metallic taste, nausea, vomiting, abdominal cramps and alas, anorexia may be troublesome for those that are compensatory eaters (143). Psychic dependence and habituation are also associated with amphetamine abuse, and the antidepressant effects of these drugs add to their abuse potential.

Although the amphetamine anorexiants generally have similar actions, differences in effectiveness and side effects have been claimed. Amphetamine-like drugs used in the United States for appetite suppression include:

1) amphetamine
2) methamphetamine
3) benzphetamine (Didrex)
4) phentermine (Ionamin, Welpo)
5) chlorphentermine (Pre—Sate)
6) diethylproprion(Tenuate,Tepanil)
7) phenmetrazine (Preludin)
8) phendimetrazine(Dietrol,Plegine)
9) mazindol (Sanorex)
10) clortermine(Voranil)
11)fenfluramine (Pondimin)

Although comparative studies show some advantage of diethylproprion in terms of side effects (29), the advantages of the

newer agents over amphetamine is not satisfactorily proven (143): Fenfluramine is a promising agent, causing drowsiness rather than restlessness and insomnia and is said to have a lower abuse potential (143, 144).

Because of their short duration of effectiveness the anorexiants can be used in several ways in a dietary program. Craddock lists the following indications: 1) to enable patient to maintain diet after initial motivation wanes; 2) to help certain depressed patients from the beginning; 3) short courses to help lose relapse weight; 4) diet failures (29). This reasonable and flexible approach emphasizes that these agents can be of use in a dietary program, but cannot be relied upon as the major contributor in weight reduction. Not only must the physician be sensitive to the fact that these agents have undesirable side effects and abuse potential, but that this form of treatment by itself offers the patient little in terms of long term weight control.

Other appetite suppressants have been used. The oral hypoglycemic biguanide, phenformin (DBI), has enjoyed some use for obese maturity-onset diabetics. Its purported success may result from its mechanism of action that lowers blood sugar without increasing endogenous or exogenous insulin, or may be a result of its side effects of ketosis, nausea, and metallic taste (143). In view of numerous contraindications and side effects, phenformin is a difficult drug to use and thus not

prescribed by many clinicians. Digitalis has been misused for weight reduction (147), anorexia being one toxic manifestation among other life-threatening ones. Its use for the treatment of obesity is irresponsible.

The treatment of obesity by hormones has maintained theoretical appeal based upon the suspicion or even conviction by many that obesity is fundamentally an abnormal metabolic and regulatory state. Thyroid hormone has received the most attention, its use in obesity based upon the increased caloric utilization affected by the hormone. Contrary to the opinion of many obese persons, the thyroid status in obesity is not different from the normal (148-151) and the metabolic rate is within normal limits (152). Abnormal thyroid function has been reported, finding that some obese have altered binding of hormone (131), and have reduced clearance of T_3 and T_4 (145, 146). Numerous studies over the last forty years have demonstrated that thyroid hormone can potentiate weight loss (153-159, 124). However, follow-up studies indicate that the losses are not maintained after the drug is stopped (158-159). This tendency to regain weight quickly is not well understood, but postulated mechanisms include a continuance of increased appetite and bad eating habits which were developed during the hypermetabolic medicated state, or a decrease in physical activity secondary to fatigue, and a temporary hypothyroidism after discontinuance of the hormone (160). Another drawback of the

thyroid hormone induced weight loss is that much of the loss is from lean body mass. Bray found about one-fifth of thyroid induced weight loss to be from adipose tissue stores (151). The negative nitrogen balance can be controlled by the use of steroids (161) or by increased protein intake (162), the latter method being far more preferable for these patients. The greatest concern for the use of thyroid hormone lies with the cardiovascular side effects. Palpitations, tachycardia, and increased blood pressure are common effects (158, 159, 151,157); cardiomegaly may occur (163) and angina pectoris has been reported in twenty per cent of one group studied (157). Urinary losses of calcium (164) may also be troublesome, possibly precipitating osteoporosis.

In sum, thyroid hormone can be used in a dieting program to produce greater weight loss, is of doubtful benefit in the long-term maintenance of weight control, and is associated with a number of troublesome and potentially dangerous side effects. Consensus opinion (165) and recent review (160) conclude that the use of thyroid hormone in the obese ought to be limited to those patients found to be hypothyroid. However, Bray claims that thyroid hormone can be used effectively. Using 100 mg of triiodothyronine daily, he found an increased metabolic rate without the extent of the untoward effects found when 150 mg or more hormone have been used (158). A high protein diet can reduce the problem of nitrogen imbalance.

Other hormones have been used. Human chorionic gonadotropin (HCG) Has received some attention since Simeons first reported its use in 1954 (166). However, that study has been criticized and subsequent trials including double-blind studies found HCG to be of no benefit in weight reduction (167,168,169). Interest has been rekindled following a recent report by Asher and Harper who administered 125U of HCG by daily injections in dieting patients for six weeks and found a significantly greater weight loss in those patients than in a placebo control group (170). However, Hirsch and Van Itallie have challenged the conclusions of this study, noting that the HCG group received more injections than the control group due to a greater drop-out rate in the latter group. They reason that the HCG group may have benefitted from the placebo effect of greater injection therapy (171). Although the mechanism of action for HCG in weight reduction is undetermined, prevention of hunger, elevation of mood (172), and thyroid stimulating activity (173, 174) have all been postulated. The burden of proof remains to establish the effectiveness of HCG, and, although it appears to be a safe agent thus far, its use should be considered experimental.

Growth hormone (GH) is known to mobilize fatty acids, to deplete fat stores without significant nitrogen loss, and reported to have a calorigenic effect through increased oxygen consumption (175, 176, 143). These actions attract theoretical interest for the use of GH in obesity. Bray administered 5 mg of GH daily to patients receiving tri-iodothyronine and found

oxygen consumption greater, nitrogen loss less, but weight loss slower than in the group receiving tri-iodthyronine without GM (161). Growth hormone appears to be well tolerated for short term usage, but long term safety (diabetogenic effect?) and effectiveness are undetermined. The present status of GH remains theoretical, as very limited supplies limit its use to restricted therapeutic trials (143).

Finally, it should be mentioned that progesterone has been found to be of some benefit for the Pickwickian syndrome (177). The mechanism involved is not known, but believed to be related to pulmonary function, not weight (178). No longer used for weight reduction is the metabolic stimulant dinitrophenol (DNP). This compound interrupts the coupling of oxidation and phosphorylation, causing generation and dissipation of heat rather than the formation of energy-rich phosphates. Use of DNP can raise the metabolic rate to about +50% and keep it at that level as long as the drug is continued. However, acute toxic effects related to hyperthermia are a hazard, as are a wide spectrum of untoward reactions associated with chronic administration of DNP. Because of the high incidence of toxic reactions and abuse of DNP, the drug is no longer used for therapy(143).

The use of drugs in the treatment of obesity remains of undramatic benefit. Amphetamines and thyroid hormones are the only agents that can be used reasonably in a weight reduction program. Utilized as adjuncts to a good diet, these agents must

be used with care in an individualized program that takes into account risks and benefits. Although there is some evidence that small dosages of thyroid hormone can potentiate the action of amphetamines (179,180), these studies are inconclusive because of the short duration of patient follow-up. Follow-up studies tend to indicate a somewhat favorable result of drug therapy as compared to only diet therapy when the follow-up time is short (181) and unfavorable results when follow-up time is longer.(182). The benefit of placebo effect need be anticipated by the physician, and initial successes ought to be put in the context of treatment risk and long term benefits.

Psychotherapy and Groups

Hilde Bruch has pointed out that obesity is associated with a number of psychological disorders rather than one (14). In light of this and in understanding the complex non-psychological aspects of the etiology of obesity, the idea of a psychotherapeutic cure for obesity seems unlikely. However, there is probably a group of patients in which emotional maladjustment is central to their obesity. Bruch has described in these patients a positive relationship between food intake and conflict situations. The obesity may either be chronic, in which case it has become part of personality development, or may be acute, a reaction to a precipitating stress. A careful psychiatric and social history will often uncover associated emotional

problems. As mentioned before, a strong relationship between physician and patient can be of great therapeutic importance, and appropriate support, understanding, and firmness has psychotherapeutic value. More serious emotional problems may require considerable time and pschotherapeutic skills, necessitating referral to the specialist. Often such patients are identified only after treatment failure or development of "dieting depression". (183). Psychotherapy is a therapeutic modality that some patients unequivocally refuse, while other more willing patients may find the expense difficult. The use of psychotropic drugs may be appropriate for some patients. Because this approach is so individualized, both diagnostically and therapeutically, analysis of results is not practical. Feinstein found psychotherapy and "mood elevation" successful for individualized cases, and possibly of benefit for maintenance (3). Clearly, some obese patients cannot successfully lose weight without adequate counseling and may in fact find dieting a severe upset to their emotional homeostasis.

Of greater interest than individual psychotherapy in the treatment of simple obesity is group therapy. The effectiveness of group therapy-like methods is widely represented by the popular private lay organizations, the so-called self-help groups, that claim a high degree of success in treating obesity. Rigorous analysis of methods and results are scantily represented in the literature for these organizations. TOPS (Take Off Pounds

Sensibly), a non-profit group operating within a model not unlike Alcoholics Anonymous, and Weight Watchers, a commercial venture, are the largest of these organizations. A number of smaller groups exist, some of which have been transiently successful commercial ventures in recent years (184).

Although the profit-making groups are generally unwilling to allow impartial researchers to study their results, there are several reports on the non-profit TOPS (185,186). Stunkard reported in 1970 that TOPS had well over a quarter of a million members in some 9500 chapters across the country. In his study of 485 members in 22 chapters in the Philadelphia area, he found membership to be comprised predominantly of white middle class women, aged 40 to 60, averaging about 60% above ideal body weight, and retaining active membership for an average 16½ months. The results were impressive. 28% lost more than 20 pounds, a figure that compares well with the medical literature on weight reduction (2). When considering only the 5 most successful chapters, 50% lost at least 20 pounds, which is as good a result as the very best reports in the medical literature. The TOPS results also fared well when considered for 40 pound loss and by the criterion of reduction index (102). Follow-up reports are lacking, but one would expect that a treatment modality that is social in nature, and realtively non-episodic in approach would stand a greater chance of long-term success than would many other methods. Questions remain, however, that make it difficult to interpret Stunkard's results. Might not

this population be an unrepresentative group of obese individuals, evidence by it being middle class, 99% female, and motivated enough to seek out the method (only 3% joined based upon physician's recommendation)?

Other reports on the self-help groups have appeared. Failures were reported by Bowser, who found group therapy no better than non-treatment control in his subjects (187), and Sussman, who reported a greater than 90% attrition rate over 6 months within a group studied (188). Equally represented were a number of positive reports of group therapy (189,190).

The fundamental aspect of the self-help approach is the use of social and peer group pressure to establish a positive attitude towards weight loss and a negative attitude towards rule-breaking and weight gain. By becoming part of the group (which usually meets weekly) a new social motivation to reduce is created. Often, the weigh-in opens each meeting in a highly ritualistic manner. Also important is the education and use of a planned but flexible diet that is rarely unduly harsh, allowing liberal amounts of food and emphasizing good food choice and reduced portions of richer foods. It allows the dieter to feel that he is not being calorically restricted (but of course, he is) and avoids the frequent association made between dieting and punishment. Discussion and sharing of relevant anecdotes can be useful, as motivation is intimately connected with group sharing and spirit. As a treatment for obesity, these groups

are less expensive than methods that require significant physician time, and also have the appeal of offering a method for long-term weight control through establishing good dietary habits and attitudes. They should be among the physician's possible alternatives for the treatment of obesity.

Behavior Modification

One of the more promising methods for the treatment of obesity to gain recent attention not unrealated to the self-help groups is that of behavior modification. Based upon the basic psychological premise that views behavior in a stimulus-response model, behavior modifiers see obesity as the result of an eating disorder which can be behaviorally manipulated. Behaviorists look at the poor long term results of other obesity out-patient therapies (2) and conclude that diet and drugs fail because patients lapse back into their former habits (100). Obesity is viewed as an addictive behavior disorder, like alcoholism and drug addiction (97), in which eating provides positive reinforcement through good taste, hunger relief, and anxiety or depression reduction. A number of behavior modification systems designed to reduce caloric intake have been described (191-197). In the medical community Albert Stunkard has emerged as the chief spokesman for behavior modification for obesity. He described this approach in four stages:

1-Description of the behavior to be controlled. Daily

records by patients of amount, time, circumstances of eating: increased awareness of quantity, speed, environmental and psychological situations associated with eating.

2-Modification and control of the discriminative stimuli governing eating. For example, time and places have become discriminative stimuli signaling eating. As in animal behavior, the stimuli come to "control" behavior. To decrease the potency of discriminative stimuli patients are encouraged to confine eating to one place (kitchen), to use distinctive table settings, and to make eating a "pure" experience (no other activities or distractions permitted.)

3-Development of techniques to control the act of eating. Specific techniques to decrease eating speed, become aware of components of eating process, and gain control (e.g. counting mouthfuls, replacing utensils onto table after mouthfuls, deliberate interruptions).

4-Prompt positive reinforcement of behaviors that delay or control eating. Reinforcement schedule, point system, money (as donations to altruistic cause). No berating for failure (183).

This technique for the treatment of obesity was first reported in 1962 by Charles Ferster, a student of B. F. Skinner (198). Interest was lacking until 1967, when Richard Stuart's paper appeared (195). Over the next seven years, Stunkard claims about ten reports appeared in the literature. He notes:"...this field has grown up largely outside of medical purview and, at

times, in the face of medical oppostions." (183) Stuart, a social worker, used behavior modification over a year and reported a greater than 20 poung weight loss for all group members (195). Although a small and uncontrolled study, the results are noteworthy in that they represent the best ever reported for outpatient treatment and by a method conducted by a man without any experience with obesity (183). Harris followed with a study using mildly obese college students, finding highly significant losses in the behavior modification group as compared to a control (194), but the study has been criticized for using as controls students who were told they were on the waiting list for treatment (183). Wollersheim's study is better controlled. Using 79 mildly overweight female college students, 4 groups of 5 members each, experienced one group treatment modality: 1-focal behavior modification; 2-non-specific, insight oriented; 3-social pressure/self-help-like TOPS; 4-deferred treatment. Behavior modification was superior to control groups (197). Hagen, with a similar population, ran ten sessions for several months with a therapist-run behavior modification group, a leaderless bibliotherapy group in which a behavior modification manual was used, and a deferred treatment control. The manual and group therapy members did equally well, averaging a 12 pound weght loss (199).

Unlike the above studies, Stunkard's patients averaged 80% overweight (191). He compared the results of behavior modification groups led by young therapists who were leading such groups

for the first time, to matched groups led by an experienced clinician with extensive experience in the treatment of obesity, Dr. Sydnor Penick, who used traditional methods of supportive psychotherapy, instruction in dieting and nutrition, and, upon demand, appetite suppressants. Not only did the behavior modification groups do better after 12 weeks of treatment for both cohorts, but one year follow-up also showed that patients at least maintained their losses. It is noteworthy that Dr. Penick's patients did impressively at one year follow-up.

Percent of groups losing specified amounts of weight (from Stunkard)

Weight Loss (lbs.)	Behavior modification groups (No.=15)		Control therapy groups (No.=17)		Ave. in medical literature at end of treatment (2)
	After treatment	1-year follow-up	After treatment	1-year follow-up	
740	13	33	0	12	5
730	33	40	0	29	-
720	53	53	24	47	25

Recently, Brightwell summarized a behavior modification technique that he considered practical for the general physician (200). He lists four criteria for patient selection: 1- 10-100% overweight; 2-desire to lose weight; 3-motivation to participate over an extended period; 4-absence of emotional or physical contraindications to weight loss. He recommends five twenty minute sessions over two to three weeks, then one session per month for follow-up, and reports good results for his group. "Such programs help patients learn how to eat properly and take responsibility for their intake". (200). Behavior modification

appears to be a superior outpatient method for weight reduction for the mildly and moderately obese. It is safe, relatively inexpensive and efficient, and in theory conducive to long term success.

Massive Obesity and Radical Treatment Methods

Based upon changing dietary habits, with or without the use of adjuncts, the reasonable treatment approaches discussed thus far, with the possible exception of thyroid hormone, ought to be viewed as relatively conservative in nature. Several radical weight reducing methods also exist. The appropriate use, as opposed to potential misuse of these methods is among the most profound challenges in contemporary medicine. It is at this point that the clinician must consider the entity of massive or morbid obesity as distinct from mild or moderate obesity. Pathophysiologically such a distinction may seem artificial, but clinical realities call for this type of diagnostic maneuvering, even if dividing lines are admittedly somewhat arbitrary. Bray warns:

> Radical methods should be employed only in massively obese patients who are severely handicapped or physically disabled by the excess weight, and only then after failure of all conservative treatment. (21)

Craddock categorizes as intractably obese those patients whose obesity is "resistant to normal methods of treatment by diet and drugs". (29) He notes that this state is commonly

associated with compensatory eating and, simplistically, in a cycle of unhappiness/love lack→eats→fat→unhappiness. Emphasizing the importance of uncovering patients' reasons for overeating and attitudes towards dieting, Craddock states that depression should be appropriately treated.

The morbidly obese patient has been defined as:

> ...one who has reached two or three or more times his ideal weight, who has maintained this level for five years or more despite efforts by himself, his family, and his physician to bring about effective and sustained reduction of weight to acceptable medical standards. (201)

A less exacting criterion commonly used for morbid/massive obesity is weighing greater than 100 pounds above ideal weight. Refractoriness to nonradical methods may have more than a merely etiologic foundation. These methods can at best reverse caloric balance to the point of a maximum adipose tissue loss of about two pounds per week and probably less because of metabolic adaptation in these patients. This rate of weight loss in a patient more than 100 pounds overweight is frustratingly slow and will rarely supply the positive feedback to maintain sufficient motivation to override the emotional and physical challenge of decreased eating. A recent editorial explains: "For the morbidly obese, 40 pounds is about the most weight that is lost and 95% of these patients will return to their previous or a higher weight within two years." (202). The following questions need be considered when evaluating the severity of obesity and appro-

priateness of radical therapy:

1) How obese does the patient measure?

2) How severe are the acute and chronic health consequences of the obesity?

3) What are the chances of success of conservative treatment? (Consider weight and treatment history, psychosocial factors, motivation and interest).

4) Do the benefits of reduction outweigh the risk of treatment?

Fasting

Physiologically, the concept of fasting is likely as old as that of diet. Anthropologically, the difference is great, as fasting since ancient to modern times has represented bodily self-sacrifice for some higher spiritual good. Willful starvation other than of the obsessional martyrdom type is seen by the medical community in patients, usually young women, with the bizarre eating disorder, anorexia nervosa. However, for the obese, fasting can maximize a negative caloric balance and has therefore been used therapeutically for obesity.

Bloom first reported fasting as an introduction to obesity treatment in 1959, when he hospitalized nine patients and fasted them for four to nine days (203). After an average loss of 2.6pounds per day - greater than accountable based upon caloric deficit alone - these patients were put on low calorie

diets as outpatients. After two to nine months, follow-up results were satisfactory. Bloom emphasizes that the fast's benefit was largely in terms of patient education, his patients learning that: 1-they could lose weight; 2-they did have will power; 3-food causes obesity; 4-they could tolerate a reducing diet; 5-they could feel well when fasting.

Keys had earlier described in his work on human starvation the absence of excessive hunger in fasting (204). The appeal of a treatment that dropped weight more quickly than dieting and could preclude the hunger problem began to attract other clinicians. In 1960 Duncan fasted fifty intractably obese subjects for four of fourteen days, achieving an average daily weight loss of 2.5 pounds (205). Vitamins and fluids were given. He noted anorexia beginning after one day of fasting, proportional to ketonemia, and reports his patients had a sense of well-being while fasting. Also noting improved patient morale after the fast, he planned weight maintenance by using intermittent short fats to prevent relapse, allowing his patients to eat freely between fasts.

Thomson reported that fasting could be effective and well tolerated for longer periods of time as in the case of one of his patients losing ninety-seven pounds in 236 days (206). He concluded that fasting is the treatment of choice for gross obesity. Eleven of Drenick's patients fasted as outpatients for twelve to one hundred and seventeen days, registering an average daily loss of 0.91 pounds (207). These patients weighed

from 240 to 550 pounds and all had medical problems. Six stopped fasting before 25days because of side effects or choosing to drop out. The average loss was about 30 pounds, the greatest 116 pounds, and initial losses were rapid (up to nine pounds in one day) and found to be proportional to initial weight. Drenick comments that the starvation was well-tolerated and contributed to these outpatients' eating habits in the future.

Several follow-up studies help us to evaluate the long-term usefulness of fasting. Hunscher's large study followed up 709 of Duncan's hospitalized fasted patients with a history of intractable obesity who were put on a reduced caloric diet and instructed to fast one day per week (208). Only 50% responded to the follow-up inquiry and of those that did, 46% lost weight, 21% stayed the same, and 33% gained since hospital discharge. The massively obese were among the most successful in the study. Hunscher concludes that two-thirds of the responders, known to be treatment failures, had benefitted from the fasting regimen. However, it would be unwise to assume that the 50% who did not respond did as well as the other group, and all that is <u>known</u> is that 23% lost weight, and 33% did not gain weight. Also of note was that 58% of the responders had follow-up durations of less than one year, where as 93% of the non-responders had follow-up periods greater than one year. Harrison followed-up 62 patients who had had a hospital stay of 10 days (209). Of thoæ one year post-fast, 40%

lost weight, while 24% of the two year follow-up group had lost weight. Fifteen patients had been fasted more than once, but did not show significantly better results. McCuish's smaller study is more discouraging (210). Twenty-five patients greater than 40% overweight with a history of treatment failure were followed-up a mean fourteen months after a successful inpatient fast for an average 25 days. All patients gained weight, the average amount of 28.5 pounds being slightly greater than the average amount lost by fasting. Because of these poor results, McCuish recommends using fasting only when some other medical reason necessitates it.

Fasting has been considered a radical method for obesity treatment because it is nutritionally drastic. Numerous physiological changes have been noted in these therapeutically starved patients, sometimes of significant clinical nature. Total starvation leads to an unavoidable protein depletion (21). Although not reported as a serious state, arrested hair growth, mild anemia and neutropenia as well as skin drying and scaling can occur. Ketonemia and ketonuria will occur, and can be used as a check for fasting adherence. Although usually mild, symptoms of unpleasant taste and nausea are not uncommon, and are thought by some to result in the hunger lack noted during fasting. The decreased hunger theory has been challenged, however, as Silverstone explains that what actually occurs is an increased hunger over the first fast day followed by a normal hunger state (211). Serum lactate levels may also be

elevated and one case of fatal lactic acidosis during fasting has been reported (212). Besides protein loss, fluid losses can also be marked, particularly early in the fast. Ball determined that for a sixteen day fast less than 15% of the weight loss was fat as compared to 70% when weight was lost by using a calorie-restricted diet (213). More prolonged fasts burn a greater percentage of fat, and analysis has determined that between 2000 and 2500 calories are lost per day (214). Reported weight losses for fasters reflect the effect of early fluid losses: 2.5 pounds average loss per day for short fasts (one to two weeks) (203,205,209) versus closer to one pound average loss for longer fasts (207,206,210). Fluid losses contribute to hypotension - orthostatic dizziness is a common minor problem-, decreased glomerular filtration (increased serum creatinine), and decreased hepatic perfusion (increased BSP retention and serum bilirubin) (21).

Potassium depletion can also be a clinical danger, and supplementary potassium chloride is recommended (21). Magnesium, calcium, and phosphorous are also in negative balance, but the depletion seems to be insignificant. Hyperuricemia commonly occurs in which case allopurinol or probenecid can be used. Blood sugar usually declines slowly, and may be as low as 40mg%, but symptoms are not reported to have occurred (21). Vitamins are needed, and one case of Wernicke's encephalopathy has been reported (215). Other problems include lassitude and weakness, constipation and, for some, a psychological reaction to fasting.

Exercise should be limited, as weakness, orthostatic hypotension, and cardiac arrhythmias may occur.

TABLE 5. Recommended Medications and Tests During prolonged Fasting. (From Bray (21))

Routine
Laxatives first 3 days
Allopurinol 600 mg/day
Vitamin and mineral capsule, 1/day
Folic acid, 5 mg/day
Bicarbonate of soda, 1 g/day
Potassium chloride solution (sugarless), 2 g/day
As Necessary
Calcium carbonate or antihistamines for nausea
Mouthwash or calorie-free chewing gum for bad-taste
Soluble bath oil for dry skin
Tests
Blood pressure, recumbent and upright, daily
Urine acetone (ketone reagent strip), daily
Serum creatinine, weekly
Serum uric acid, weekly

Bray recommends that fasting not be continued for more than two months, as some side effects are more evident as the starvation is prolonged (21). Long-term effects from the metabolic changes of fasting are yet unknown. Contraindications to fasting mostly follow logically from the observed metabolic changes and the nutritional consequences of starvation: pregnancy, peptic ulcer, hepatic insuffiency, labile diabetes mellitus, gout or hyperuricemia. General mental and physical health must be considered, and the importance of heart disease is indicated by the report of two deaths in fasters with left ventricular failure (216). Refeeding after fast is best gradual. Fluid retention may be marked, and a post-fast weight gain should be expected. Salt restriction may be beneficial.

It has been suggested that perhaps some of the metabolic derangements and dangers of fasting could be avoided with the use of a semi-starvation regimen. Genuth found a lessening of hypoglycemia, ketosis, hyperuricemia, and urinary losses of potassium and phosphorous by adding to the fast only 50 grams per day of L-alanine, a glucose precursor (217). He also reports a persistence of anorexia when L-alanine, glucose, or casein calcium (milk protein) are used for 200 to 300 calories per day. In a program for 75 massively obese patients (average 196% ideal weight), Genuth followed a completely foodless week of hospitalization with a semistarvation regimen consisting of 45 grams of casein calcium (Casec) and 30 grams of glucose daily for eight to fifty weeks as outpatients with close monitoring (218). Protein sparing through the use of small amounts of exogenous protein had been previously documented (219,220), and daily casein had been used in fasters who continued to lose weight but maintained nitrogen balance (220). 60% of Genuth's patients lost 40 pounds or more, the average loss being 85 pounds. Losses averaged about four pounds per week. 37% of the patients were defined as failures: did not last eight weeks or did not average two pounds per week loss. Most failures had vague symptoms from the withdrawal of food. No severe chemical derangements occurred, and a modest catabolic state with small potassium and phosphorous losses did not prevent patients from having normal activities. Uric acid

and B-hydroxybutyrate elevations were measured but were well below fasting levels.

Fasting is an effective method for relatively rapid weight loss. After careful initial screening to exclude those patients for whom the physiologic stress of starvation would be dangerous, an inpatient fasting regimen can be well tolerated if close medical monitoring and appropriate preventive treatment are provided. Minor complaints are common, and life-threatening problems are uncommon but do occur. The contribution fasting makes to long-term obesity management is still uncertain, but most studies indicate modest long-term benefit for the intractably obese. Outpatient fasting as a method more reasonable than periodic inpatient fasting is not ideal because of the looser patient supervision and the marked fluid and protein shifts associated with the onset of fasting. Low protein/glucose semistarvation regimens appear promising and may prove useful and relatively safe for a segment of the massively obese outpatient population that can comply with the freedom of an outpatient regimen. In sum, fasting may be indicated for the massively obese, the intractably obese, or the obese patient who requires a rapid weight loss for medical reasons. It is of best use for rapid weight loss and of less clear benefit for long-term management. If time permits, apropriate patients may be better treated with outpatient semistarvation. As always, risks of this radical treatment must be

weighed against expected benefits.

Surgery

Obesity can be a chronic disorder, refractory to medical treatment, and particularly when massive, may be clearly life-threatening. Surgery as a last resort to produce a negative caloric balance and maintain weight control may be appropriate for some patients as indicated by the opinion stated in a recent editorial: "There is no satisfactory nonoperative treatment for morbid obesity." (202). The intestinal bypass has been the surgical procedure to receive the greatest attention, the basic principle being that of decreased nutrient absorption due to a surgically reduced intestinal absorptive surface. Kremen's experimental report of jejunoileostomy appeared in 1954 (221), and was soon followed by Payne's series of 90% bypass jejunocolostomies (222). Although fine weight losses were achieved, the morbidity was prohibitive, as severe diarrhea, electrolyte abnormalities, and liver pathology were seen and one death was reported. Reanastomosis in a second surgical procedure was recommended. By the mid - 60's the medical community had denounced the bypass as an unsafe approach to obesity (223). Nevertheless, some surgery continued to be done, reports appeared, experience was gained, and techniques improved (224 - 230). The jejunoileostomy emerged as the

best procedure, a less radical bypass that could achieve a balance between intake and weight loss without the need of a second surgical procedure. Recent articles estimate that about 1000 cases have been published in more than two dozen series and the the total bypasses performed is probably several times this figure (229,230). The most popular procedure is that developed by Payne and DeWind (225) in which an end to side anastomosis is made between 14 inches of jejunum proximally and the last 4 inches of terminal ileum distally, allowing for some ileal absorption and leaving the ileo-cecal valve intact. The bypassed intestinal segment remains in situ closed at the jejunal end, and may be involved in the variable absorption seen, as a result of ileal reflux. Modifications have been developed with some good results. The end to end jejunoileostomy is claimed theoretically good for lowering hyperlipidemia (225), and has also been reported to produce better weight loss than the end to side procedure (231).

Postoperatively an adaptation period occurs in which the remaining absorptive intestinal surface hypertrophies and weight eventually levels off at a point somewhat above the ideal. Weight losses for the first year are generally reported to be between 85 and 100 pounds, greatest during the first six months, and proportional to the initial weight (231, 21, 229, 232). This represents about a 30% weight loss. Second year losses are reported to average about 50 pounds; third year average about 25 pounds, and one study found an average nine pounds lost

during a fourth postoperative year (231). Buchwald averaged the weight losses reported in nine series and found jejunoileostomy produced 35% weight loss (follow-up times varied, though) as compared to 41% weight loss for a small series of jejunocolostomies (225). Salmon reports that two-thirds of his patients plateaued at weights within twenty pounds of ideal at one to three years follow-up (228), while Buchwald reports that 90% of his 94 patients reached within 50 pounds of their ideal weight (230). A few patients will not successfully lose an adequate amount, varying from one series to another (228,229). Bray notes that the weight loss in bypass patients is slightly slower than that achieved by fasting (21).

The evident success in losing and maintaining weight for the massively obese patient with the intestinal bypass must be measured against the morbidity and mortality that results from this procedure. Operative and early postoperative mortality has been variously reported between 0.7% and 6% for a number of the larger series (225, 228, 230, 222, 202), as pulmonary emboli, cardiac failure, myocardial infarction, and wound infections are most commonly involved. Payne, who reports on 165 of his patients operated on over a 16 year span, found a total mortality of 9.7%, but only 6% that could be attributed to the bypass, with hepatic failure as the most common cause (222).

The side effects of intestinal bypass are considerable. The average postoperative hospital stay was 10.5 days in one large

series, and non-fatal surgical complications of wound problems, upper gastrointestinal bleed, urinary tract infection, pulmonary embolus, thrombophlebitis, and pneumonitis are reported in a minority of patients (230). Longer term effects experienced by nearly all patients include diarrhea, electrolyte abnormalities, and deficient vitamin B12 absorption. The diarrhea tends to taper off after a 3 to 6 month period during which nearly every patient experiences the troublesome symptom, with up to 30 liquid stools per day reported (229). Related problems of anal pain, hemorrhoids, proctitis, and fissures can make this a difficult period. Salmon reports that 39% of his patients had diarrhea (3 liquid stools per day) at 6 months, 25% at one year, and 13% at two years (228). Special diets can help, as can antidiarrheal agents. Although the diarrhea is usually controlled with time, dietary indiscretion may cause recurrence. Hypokalemia and hypocalcemia are frequent in the early postoperative period, when absorption is very low. One hypocalcemic death has been reported and another series reported hypocalcemic tetany in 3 of 140 cases (230). Prophylactic therapy using Lomotil, calcium carbonate, potassium, multivitamins, and B12 injections has been recommended (229). Fatigue, thirst, nausea, abdominal pain, and small gastrointestinal bleeds seen in the early postoperative period are usually well controlled. Hair loss occurs in about 3%, but recovery is after several months.

A number of long-term complications exist. Of greatest interest has been the effect of bypass on the liver. Reports of hepatic failure and death (225) led to the conclusion that the bypass produces liver disease and is more hazardous than anticipated (233). However, it was noted that it had previously been determined that liver function was abnormal in massive obesity (234) and that 75% of the patients undergoing bypasses have fatty livers preoperatively (235). Postoperatively, fatty changes are variable and unpredictable (222). A recent study reports that twelve of eighteen patients had an elevated SGOT and biopsy proven worsened fatty liver four months postoperatively, and also showed amino acid deficiencies in a profile typical of protein-calorie malnutrition. Between 12 and 36 months postoperatively weight stabilized, SGOT returned to normal, hepatic fat diminished, and amino acids improved, all, presumedly, as a result of increased intestinal absorption (236). Post-operative amino acid supplementation is proposed as a means to protect the liver. Evidence supports the fact that after a period of postoperative challenge, the liver goes on to improve and may be improved from its preoperative state (237,236).

Other long-term complications include those that can result from the intestinal surgery: adhesions, obstruction, and rarely intussusception. Polyarthritis has been reported, and may be severe (230). As with fasting, gout and hypotension

may be precipitated. Other hazards include renal calculi, gastric stress ulcers, duodenal ulcers, cholelithiasis, and a hyperchloremic acidosis with renal impairment. Intractable nausea and vomitting can be severe, leading to malnutrition and electrolyte imbalance. If a complication is severe enough and potentially reversible, reanastomosis may be indicated, as Payne found it necessary to reanastomose four of 153 jejunoileostomies because of intractable electrolyte imbalance and severe liver changes (231).

The risks and ill effects of intestinal bypass are impressive. Indications and contraindications for this surgery are generally cautiously expressed with this in mind. The following include criteria for surgery usually mentioned: 1-massive obesity, usually of long duration; 2-a history of multi-treatment failure; 3-medical complications of obesity; 4-emotional stability, cooperation, and motivation; 5-full informed consent. The last item is of great importance, as patients must understand what risks and responsibilities they are taking. An experienced and available medical and surgical team might be added to the criteria list, as the long-term responsibilities of the providers are considerable. Contraindications are relative, but in general reflect an attempt to protect the highest risk group from the hazards of the bypass. Often mentioned are liver abnormalities, advanced age, emotional instability, hostility, unwillingness to stop

all alcoholic intake, unrealistic expectations, and conditions that would be too risky for a major surgical procedure.

The primary benefit of intestinal bypass is irreversible weight loss and weight control. Related benefits are decreased blood pressure (75% preoperatively are hypertensive (230),) improved respiratory and cardiovascular function, limitation of diabetes mellitus (8% preoperatively diabetic), improved arthritis, improved fertility, decreased serum cholesterol, and improved psychological situation. The weight loss is also beneficial against other obesity hazards that may now be prevented. Solow examined the psychological effects of intestinal bypass by studying 24 patients who had had the operation (238). Improvement in mood, self-esteem, interpersonal and vocational effectiveness, body image and activity levels were found, and the decrease in depression and improvements in ego strength were directly proportional to the magnitude of weight loss.

Appropriate use of the intestinal bypass for obese patients is a great challenge. In making this decision the following questions may be helpful in the context of risk-benefit model:

1- How obese is the patient?

2- How great is the debilitation or risk caused by obesity?

3- Have other methods been given an adequate trial?

4- Is he a good candidate in terms of the physical and mental stresses of this procedure?

There clearly seems to be a population of massively obese patients for which the intestinal bypass is the treatment of choice. It is, though, because of its high risks, the treatment of last resort. One recent concern expressed has been that general surgeons will take this procedure lightly and perform too many (239). This would be tragic. However, a good number of medical centers have the facilities, manpower, and professional expertise to successfully integrate surgery, medicine and psychiatry into a team to work with bypass patients. To not answer this therapeutic need would be a grave omission for a qualified medical center.

Another surgical approach to obesity is that of gastric surgery. Either by gastroplasty or a gastric bypass that excludes the distal 90% of the stomach, the small stomach reservoir insures limited food intake through the deterrent of the dumping syndrome. Mason, who has had the greatest reported experience with the gastric bypass, found weight losses for his patients comparable to those found in the intestinal bypass literature, and with less mortality and morbidity (240, 241). The 4.6% overall mortality for the gastric bypass, however, is reduced to 2% for the gastroplasty, although the weight losses seem less reliable after the latter procedure. Fundamentally, the gastric procedure patients are less disabled than those with the intestinal bypass because the former only limits intake,

while the latter limits absorption (202). Although a less proven procedure, the gastric bypass or gastroplasty ought to be considered as an alternative to the intestinal bypass, and may be particularly useful for those massively obese patients for whom the malabsorptive side effects of the intestinal bypass would be prohibitive.

Numerous other treatment methods have been used for obesity. Those reviewed here, it was judged, represent the mainstream of the medical art of obesity therapy. Undoubtedly, other methods have often been used successfully if only infrequently. A new and novel method often has an appeal advantage over a more traditional one. Methods such as hypnosis and fad diets can be successful in the short-term but there is little evidence supporting their effectiveness for long-term weight control. (3) In addition to novel approaches that actually have some pathophysiologic basis, there are others that do not. Weight reduction is a big business, and profit-seeking in this field is a strong incentive to push a reduction method or adjunct regardless of its proven effectiveness. Furthermore, obese patients are often prime candidates for quackery when a personal history of failure exists and the physician-patient rapport has been tarnished. A physician can best protect his patients from quackery by maintaining an educating, sympathetic, and supportive role.

Summary and Conclusions

The definition, measurement, prevalence, hazards, categorization, and etiology of obesity were reviewed in the previous section. It was concluded that obesity is a pathological entity which is clinically measurable and carries with it distinct risks and consequences to one's physical, emotional, and social well-being. The risks and consequences are numerous and varied, are often of unclear connection to the obese state, and vary in reversibility resulting from weight reduction. Evidence favors the conclusion that weight reduction is desirable for many and probably most obese individuals. The risks of obesity generally are proportional to the degree of adiposity, and weight loss can be urgently needed especially in massively obese patients and those with medical complications.

As the etiology thus far determined is multiple and complex, it is not surprising that multiple therapeutic approaches would be available. The principles, methods, effectiveness, hazards, indications and contraindication for the treatments for obesity have been discussed in this section. Numerous approaches exist, reflecting the various etiologic influences, and differ, to some extent, in terms of short- and long- term effectiveness and hazards. All methods carry some risks and costs, varying in a spectrum from the most benign and conservative to the most radical. It has been stressed that because different treatment schemes are best applied to different patients, the physi-

cian should take a dynamic and flexible approach in which risks and consequences of nontreatment are comparatively considered against the risks, costs, and long- and short- term benefits of various treatment modalities. The following table may serve as a guide to quickly generalize the hazards and benefits of different treatments.

TABLE 6

TREATMENT	ADVERSE RISKS AND CONSEQUENCES	COSTS AND INCONVENIENCE	SHORT TERM SUCCESS	LONG TERM SUCCESS
	(0-5)			
Low calorie diet	1	1	1	1
Free diet	1	1	2	1
Self-help groups	1	1-2	3	?2
Behavior modification	1	1-2	3	?3
Psychotherapy	1	3	1	?2
Amphetamines/diet	2	2	2	1
Thyroid/diet	3	2	3	1
Fast	4	4	5	2
Bypass	5	5	4	5

The above chart is limited in usefulness in that it cannot take into account the specific case of the patient for whom treatment is being considered. Several points are worthy of further consideration.

ADVERSE RISKS AND CONSEQUENCES. Every treatment carries with it at least some risk, as the change in eating behavior required for even the most benign treatments can be a psychological stress for some obese patients. If the patient for whom conservative treatment might precipitate a "dieting depression" can be identified during pre- or early treatment, then a decision not to treat such an obese individual might be appropriately made.

COSTS AND INCONVENIENCE. A low calorie or free diet requires ongoing support and follow-up by a physician, nutritionist or other health care provider. If drugs are added to the program, both patient responsibility and physician/provider time may be increased. Self-help groups are generally less expensive on even a weekly basis than less frequent physician visits, and members often view the meetings as socially pleasurable rather than inconvenient. However, for some, an added dimension of compliance beyond just diet makes the self-help groups somewhat more inconvenient. This is especially true for men, who rarely find these groups satisfying and effective. Behavior modification generally requires a leader's time - not necessarily a physician - with some understanding of the treatment method. However, bibliotherapy may prove to be an efficient alternative requiring a minimum of professional services. For the patient, it would seem that compliance with behavior modification methods would be of moderate inconvenience. Psychotherapy is an ongoing procedure which is quite costly, in most cases. Fasting is

highly inconvenient and costly on an inpatient basis, but much less so if feasible as an outpatient. Surgical bypass is far greater in terms of cost and inconvenience than any other method.

SHORT TERM SUCCESS. Individual successes vary, and the chart does not take into account, for example, the patient who will do better with the rigid guidelines of a strict low calorie diet as opposed to the more liberal approach of the self-help groups. The hysterical personality style may respond quite differently to a treatment approach than an obsessive-compulsive. It is a challenge for the physician to provide a regimen for his patient that is sufficiently individually syntonic with his character, needs, and motivation to maximize chances for success. Furthermore, chances of success can be increased considerably by factors intrinsic to the physician-patient relationship. These variable constant, evidence suggests that the short-term success of the traditional conservative treatment methods (diets, amphetamines, psychotherapy) are generally poor to fair. The newer and less researched conservative mthods (self-help groups and behavior modification) are generally more promising. Only the fast and bypass have proven to be reliable methods for weight loss.

LONG TERM SUCCESS. Of greatest importance in the treatment of obesity is the long-term success. Unfortunately, much less is known about the long-term effectiveness of different methods than the short-term success. While the latter is often

moderately good with conservative methods, the former has traditionally been poor. Conservative methods that help change eating habits and behavior would seem to offer some advantages towards long-term weight control, but few studies have been conducted to verify this. There is little to lead one to suspect that fasting is especially effective in the long run. The only treatment for obesity known to be on long-term effectiveness is surgery.

SUMMARY OF SUGGESTED TREATMENTS FOR PATIENTS OF VARYING DEGREES OF OBESITY

Mild-moderate obesity (0-20% overweight)

1-Self-help groups. If a quality organization exists in the community, this may be considered a first-line approach for women with mild to moderate obesity. Patient interest as a prerequisite, the physician ought to take the responsibility of patient follow-up and continued support so that another method can be used if this approach fails. Occasionally, men interested in these groups (such as Weight Watchers or TOPS) may be good candidates.

2-Behavior modification. This newly utilized approach appears to be the treatment of choice for mild to moderate obesity. Unfortunately, the availability of this method for obese patients remains very limited at this time. It is hoped that the resources will be rapidly developed so that patients can benefit from this promising approach to obesity.

3-Low calorie diet. A safe and simple approach, it may be effective with some patients, particularly those most motivated, but usually is ineffective. Physician support is important.

4-Free diets. Also safe and simple, some patients will do well, particularly those well-motivated and within the context of strong physician-patient rapport. Long-term management is generally poor.

5-Amphetamines/diet. Anorexiants may be used as adjuncts for these patients, particularly to help a patient start a "difficult" diet. Generally, these agents offer little above diet alone for long-term weight control.

6-Psychotherapy, thyroid, fasting, surgery. These more hazardous and/or costly methods can rarely be justified to treat this group of obese patients.

Moderate-severe obesity
(20%-40% overweight)

1-Self-help groups. These groups may be effective for these patients, particularly women who have had previous success with them.

2-Behavior modification. Although only several studies exist, behavior modification is probably the best first line treatment when available for this group of patients.

3-Low calorie or free diet. Few patients in this group will succeed on these regimens. However, some highly motivated

patients may, and more hazardous treatments may prove unnecessary. Recurrence is very high.

4-Amphetamines/diet. Some patients may benefit from the gratification of more rapid weight loss that these drugs may contribute to, but for most patients, the benefit of adding amphetamines to a good diet regimen is marginal.

5-Thyroid/diet. For carefully selected patients with close supervision, thyroid hormone may be used to contribute a successful weight loss. However, cessation of hormone treatment may lead to greater difficulty in maintaining the loss.

6-Fasting. Inpatient starvation is severe treatment for these patients, but where rapid weight loss is strongly indicated, it may be necessary. Outpatient fasting or semistarvation is also rather severe, but could be well worthwhile for those patients for whom the above methods have failed, are contraindicated, or unavailable.

7-Psychotherapy. This may be of great importance for certain patients for whom conservative treatment failure is evident and psychologic factors appear to be dominant. Unfortunately, both patient refusal and high cost of treatment often necessitate that this modality be underutilized. Of course, psychotherapy is only an adjunct to a weight reduction method.

8-Surgical bypass. This hazardous approach would rarely, if ever, be indicated for this population.

Severe obesity
(40%-60% overweight)

1-Self-help groups, diets, amphetamines. Only occasionally will patients of this degree of obesity do well with these regimens. They require large weight losses for adequate treatment, and recurrence is likely. If treatment failure has not occurred in the past with these conservative methods, a treatment trial may be worthwhile with the hope that more radical methods may be avoided. However, most of these patients have a history of failure with these methods.

2-Behavior modification. There is some evidence that this approach may be effective for this group. Further experience will better resolve this issue, but at this point in time a trial of behavior modification could be worthwhile.

3-Thyroid/diet. Although more hazardous than conservative measures, thyroid can be an effective adjunct to diet contributing to a successful weight loss. However, it has little or nothing to offer above more conservative methods for long-term weight control.

4-Fasting. If conservative treatment methods fail, these patients ought to be considered for a period of supervised starvation or semistarvation. For most, a semistarvation trial (a promising method by recent reports) would not be unreasonable. For many, including those for whom outpatient semistarvation is not successful, a supervised hospitalized fast should be tried with the hope that this successful weight loss will be maintained.

5-Psychotherapy. Counseling is probably indicated for most patients in this group with a history of treatment failure. Unfortunately, this is often not practical or possible.

6-Surgical bypass. Surgery may be indicated for some patients in this group. Not only must their obesity be of sufficient severity and consequence to their well-being, but also a documented history over a period of years of treatment failure with conservative methods, fasting, and preferably, psychotherapy. Of course, motivation and full informed consent are also prerequisites.

Massive obesity
(> 60% overweight)

1-Self-help groups, diets, amphetamines, thyroid. These treatments will only rarely be of significant benefit for the massively obese. However, if conservative methods have not been tried, there is little to lose by initiating a trial for a limited period of time. Strong physician support is needed if a conservative method is to have any chance of success. Even if weight loss is achieved, recurrence is likely.

2-Behavior modification. Evidence is lacking as to whether this method is of use for this group. However, since it is benign and early reports have been promising for its usefulness in the moderately obese, a trial may be worthwhile.

3-Fasting. Fasting should be considered an indicated treatment for these patients after a history of treatment failure with more conservative measures. With the help of counseling and

support, and other learned means of weight control, it is hoped that surgery will not be necessary.

4-Psychotherapy. Most of these patients could potentially benefit from the insight gained through this therapy. Psychotherapy should be considered an important, if not necessary, adjunct to weight reduction therapy for the massively obese. Of course, some patients may refuse this therapy.

5-Surgical bypass. This "last resort" treatment may be indicated in a fair proportion of the massively obese group. A history of treatment failure including conservative approaches, fasting, and psychotherapy should be documented, as well as a clear and serious health threat as a result of intractable massive obesity.

Obesity, is a potentially treatable disorder that produces a variable but definite hazard to the health and well-being of an individual. The physician has the responsibility to devise a treatment program in conjunction with his obese patient that is in the best interest of the patient. Although successful treatment is difficult to achieve, particularly in the long run, a number of different treatment approaches can be used. Used appropriately in a conscientious program of ongoing commitment, the chances for successful treatment are maximized and, it is proposed, greater than that that has traditionally been achieved.

A FOLLOW-UP STUDY OF FASTED PATIENTS

INTRODUCTION

The treatment of obesity has been reviewed in the previous sections. It was concluded that simple obesity is a complex state resulting from a positive caloric balance but contributed to by multiple inputs. Likewise, a variety of treatment approaches are available that can be used to maximum effectiveness when a thorough knowledge of both patient and treatment method exist. Massive obesity, previously defined, poses a great challenge to the physician as these unfortunate patients carry the greatest risks and consequences from their obese state and are usually refractory to conservative weight reduction methods. Fasting has developed as a major means of medical management for the intractable massively obese. As previously discussed, fasting has been in reported use for over fifteen years, during

which time its effectiveness for rapid weight loss has been well documented. (203, 205-207). Used in a hospital setting with careful supervision, the fast is generally well-tolerated, although minor side effects are common, the nutritional state is drastic, and, rarely, life-threatening complications will occur (21, 212, 213, 215, 216). In a program in which patients are well-screened, inpatient monitoring appropriately executed, and preventive measures taken, most complications can be prevented or well-controlled. Although most fasts are terminated within two months, longer fasts have been reported and well-tolerated (21, 206).

While the reliability of acute weight loss for hospitalized fasters is good, the benefit of fasting for long-term weight control is far less clear. Some authors have claimed that their fasted patients received benefit beyond the fasting weight loss in that positive feedback from a successful loss, changed eating habits, and the ease of not eating were important learned experiences contributing to long-term weight control (203, 205, 207, 208). However, the few follow-up studies found in the literature show modes and inconsistent long-term weight control for those fasted (208-210). While the inpatient phase of weight loss is rather easily executed with consistent success, the outpatient post-fast period is far more variable in terms of patient reponsiveness, appropriate treatment and the multitude of factors that can influence success.

This study follows up a group of thirteen patients who had been fasted for varying periods of time as inpatients on a metabolic research ward. In addition to information directly related to post-fast weight control, other issues related to the history, etiology, consequences, habits, hopes, expectations, knowledge and insight pertinent to obesity in these patients was explored. These results will be contrasted to our present understanding of the obese patient and his management. It is hoped that such information can contribute to the successful management of obese patients on an individualized basis and also help illuminate important common characteristics of the severely obese.

PATIENTS AND METHODS

Thirteen patients had been fasted on a metabolic research ward at Yale-New Haven Hospital for varying lengths of time within the period from November 1973 to November 1974. All were under the care of Dr. Robert Sherwin, a metabolic fellow (under the supervision of Dr. Philip Felig) and later an assistant professor of medicine at the Yale Medical School. Patients were referred to Dr. Sherwin via several routes, and were screened by the following criteria: 1-rule out unhealthy (flexible), especially those with severe hypertension, heart disease, diabetes mellitus, or gout; 2-preferably young; 3-preferable at least 50% overweight; 4-motivated to lose weight by fasting. Prospective patients were to understand and consent

to an inpatient stay which included within it a fast and also metabolic studies requiring either ketone infusions that were to test the effects of ketone acids on urea nitrogen excretion and circulating amino acids or glucagon infusions that were to test the effects of fasting on glucagon kinetics. All patient costs were covered through research funds. After full informed consent, patients were admitted to a research ward which was predominantly filled with non-obese patients suffering from other ailments. Patients were first placed on a calorically controlled maintenance diet (generally 3000 calories) for various lengths of time, and then fasted with 0 calories for duration varying between 17 and 70 days. One patient was calorically restricted for an extended period before fasting was begun. All admitted patients received complete histories and physical examinations. Electrolytes, calcium, phosphorous, magnesium, liver and renal function, protein, thyroid, and blood count were measured periodically. Patients were weighed daily. While fasting, patients were given daily 2 liters of water (minimum), multivitamins, 1 mg of folic acid, 625 mg sodium bicarbonate, intermittent potassium supplements as needed, allopurinal if hyperuricemic, and supplemental salt if orthostatic hypertension occurred. Patients were seen daily by Dr. Sherwin, who would spend on average about twenty minutes with each patient. Psychiatric consultation was sometimes used, and counseling (in addition to Dr. Shwerwin's role) was often recommended. Fasting was generally terminated when metabolic

studies were complete. Patients were then placed on a 150 to 200 calorie diet and were gradually increased to a regimen of 600 calories over a period varying from one to three weeks and then discharged. As outpatients, patients were instructed to use diets generally between 600 and 1000 calories. Dr. Sherwin followed all these patients, seeing them on a flexible schedule of once per week or less frequently.

All thirteen medical records were reviewed for data related to the fasting hospitalization. Follow-up data was not consistently available in the medical record. With Dr. Sherwin's cooperation, an attempt was made to plan an interview between each patient and the author at the Yale-New Haven Medical Center. Through a planned but flexible format of questions, the interview would explore relevant areas of weight and treatment history, the personal consequences of obesity, eating and exercise habits, the fasting experience, the follow-up period, and personal opinions and insights about the treatment of obesity and their weight problem. The length of the interview would vary between 45 and 90 minutes. The research protocol was reviewed and accepted by the Yale Human Investigation Committee. An outline of questions covered in the interview appears in the appendix.

RESULTS

THE FAST AND FOLLOW-UP

Medical records were reviewed for all thirteen patients

and data was collected for age, fasting dates, admission weight, pre- and post-fast weight, and hospital course. Follow-up data was available only through patients interviews of Dr. Sherwin's private records. Patients ranged between 19 and 51 years of age, with a mean age of 31.6 . Eight were women, with an average weight of 251 pounds, and a range of 182 to 350 pounds. Five men were fasted, averaging 463 pounds with a range of 310 to 655 pounds. The average weight for all 13 patients was 308 pounds while the median was 264. The degree of obesity expressed as a percentage above maximum ideal weight was calculated. Using height and weight tables and assuming large frame body type the % overweight ranged from 20% to 206% with an average value of 88% and a median of 86%. Fasts ranged from 17 to 70 days, with a mean and median of 34.6 and 31.5 days respectively. The patient who fasted 17 days terminated his fast by eating for several days while out of the hospital on pass. He returned to the hospital 20 pounds heavier and renewed his fast for another 23 days. All other patients completed their fasts successfully, terminating according to physicain orders. Minor cheating episodes were occasionally reported, but did not seem to significantly affect weight loss rates. Patients were frequently granted passes to leave the hospital when it was important for them to do so. Weight loss by fasting averaged 43.4, with a median of 40 and range of 20 to 71 pounds. The average loss per day was 1.27. Loss per day was calculated to correlate with initial weight with an r value of

+0.64 ($p < 0.05$). (All computation schemes in appendix). The correlation between loss per day and days fasted calculated to $r = -0.62$ ($p < 0.02$). All thirteen patients lost more than 20 pounds, and 8/13 lost 40 or more pounds. Reduction indices ranged between 36 and 94, with a mean of 63 and a median of 66.

Up to date follow-up data was available for 8 patients. For the five patients for whom current weights were not available, a follow-up weight for their last physician visit was available for all but one. Follow-up duration ranged between 0 and 15 months, with a mean of 7.1 and median of 8 months. Follow-up weight change ranged between 43 pounds lost to 255 pounds gained, with a mean of 29.8 pounds gained and a median of 0 (no weight change). Expressed as a function of time, the monthly weight change ranged from 4.4 pounds lost to 23.2 pounds gained, with a mean value of 4.2 pounds gained and a median of 0.3 pounds gained. Testing correlation between duration of follow-up and weight change (gain) for these patients, an r value of +0.47 was calculated ($p < 0.10$). For the 8 patients with up-to-date follow-up data the mean follow-up interval is 8.3 months, the mean weight change is 17.1 pounds gained and the mean monthly change is 2.1 pounds gained.

Interviews were held with 8 of the 13 patients. All five of the non-interviewed patients are currently lost to Dr.Sherwin's follow-up. Only one of the eight interviewed had stopped seeing him. No patients refused to be interviewed, but 5 were unable

TABLE 7

FASTING AND FOLLOW-UP DATA FOR 13 PATIENTS

Patient	Admission Weight	% Over-weight	Duration	FAST			FOLLOW-UP		
				Loss	Loss / Day	Reduction Index	Weight Change	Duration	Change / Month
1*	324	78	42	53	1.26	68.5	+70	11	+6.4
2*	264	94	46	42	0.91	61.8	-16	5	-3.2
3*	253	58	28	24	0.86	46.5	+45	13	+3.5
4*	310	78	21	40	1.90	52.1	- 4	2.5	-1.6
5*	373	86	21	40	1.90	41.4	-11	2.5	-4.4
6*	350	151	42	57	1.36	65.7	+39	6.5	+6.0
7*	256	86	28	42	1.50	66.0	-43	11	-3.9
8*	332	89	36	43	1.19	52.0	+57	15	+3.8
9	182	25	24	24	1.00	83.1	0	2	0
10	185	20	35	20	0.57	77.5	+ 4	8	+0.5
11	261	74	51	47	0.92	73.7	- 4	5	-0.8
12	260	98	70	61	0.87	93.9	0	0	---
13	655	206	17,23	35,36	2.06 / 1.50	36.1	+255	11	+23.2

*Patients interviewed, Follow-up data Up-To-Date

to be located or reached. The mean duration of time from hospital discharge to the date of this study (interviews) is 12 months for those not interviewed and 8 months for those interviewed. All of the following data was collected only from the 8 interviewed patients.

Major reason for seeking treatment by fasting: health or physical problems -4, desperation -2, job requirement -1, self-satisfaction -1.

Hopes and expectations for fast: 30 to 70 pound weight loss -6, to successfully eat nothing -1, no expectations -1. 3/8 of the patients mentioned continued weight loss after fasting as a major expectation.

Fears of fasting: none-4, intravenous infusions -2, failure -1, regain of weight -1.

General quality of fasting experience: easy or well-accepted -7, bad experience -1. The latter patient described the fast period as "one of the most difficult experiences in my life."

Best aspect of fasting experience: weight loss and/or ability to lose weight -4, interactions with fellow obese patients -2, nothing -2.

Worst aspects of fasting experience: emotional difficulties -4, boredom or confinement -5, physical difficulties -4. Of these latter 4 patients, 3 had some problem with orthostatic hypotension and 2 had muscle spasms after receiving a ketone infusion (1 of these patients had hyperventilated). Difficulty

coping with very ill or non-fasting patients on ward -3, coping with forced regimen -1.

Hunger: none -3, several days -3, one week -1, entire fast -1.

Post-fast change in eating habits: none -3, slight -2, follows diet -1, can eat considerably less -2.

Use of diet: poor or no adherence -3, moderate adherence (500 calorie) -1, generally good adherence (600-800 calories or free diet) -4.

Frequency of medical follow-up: regular and at least once/ 6weeks -4, irregular and rare -3, presently lost to follow-up -1. The average post-fast weight change for the four patients who regularly see their physician is -18.50 pounds. For the other four patients the average is +52.75 pounds.

Purpose of follow-up visits: general support for weight control -5, check weight and diet -2, not sure -1.

General satisfaction with fasting as treatment for obesity: yes - 6, no - 2. The most successful post-fast weight loser felt that the fast was a good way to start a big weight reduction, proving to herself that she could lose weight and feel better. Two patients felt that fasting was emotionally difficult. One faster criticized the method because it doesn't get to the root of the problem. "I can't fast my entire life," he said.

WEIGHT HISTORY.

Family: both parents obese -4, only one parent obese (mother) -4.

Obesity onset: infancy and early childhood -3, late childhood and early adolescence -2, late adolescence and early adulthood -3.

Precipitating events for weight gain: emotional stress-7, Of these 7 patients 4 were able to specify important life events that preceded significant weight gain. Pregnancy -1, none -1.

Pattern of weight change since onset: constant gradual gain -1, gradual gain with plateaus -2, gradual gain with marked spurts -2, gradual gain with intermittent losses -3.

Previous treatments for obesity: low calorie or free diet -8, fad diets -3, psychiatric counseling -4, amphetamines-7, thyroid -1, Weight Watchers -4, ? injection therapy -1, hypnosis -1, heat therapy -1, previous fast -2.

Best treatment method experienced to date: fast -6, free diet -1, Weight Watchers -1.

Worst treatment method experienced: fast -4, amphetamines -2, low calorie diet -1, not sure -1.

The ideal way to lose weight: a pill that burns up calories -3, don't know -3, stop eating -1, good habits/prevention -1.

EATING AND EXERCISE HABITS.

Number of regular meals per day: none-2, one -1, two -2, three -3.

Quantity of intake: very large -4, moderately large -4.

Snacking habits: considerable snacking -8. 5 of these patients indentified the evening, one named the mid-afternoon, and two anytime as the periods during which they snacked the most.

Food preference: none particularly -3, tasty and savory foods, not sweet or heavily spiced -4, sweets -1.

Importance of eating habits for weight control: very important -6, moderately important -2.

Are your habits conducive to weight gain?: yes - 8.

Exercise amount: none-2, very little -5, moderate -1.

Exercise enjoyment: dislikes -2, mixed feelings -4, likes -2.

CONSEQUENCES OF OBESITY.

Effects on social life and emotional well-being: public ostracism -4, self-image -2, job pressure -2, romantic life -2, compensatory personality development -2, affects entire life -1, no effects -1.

Improvement of above effects after successful weight loss: yes -4, partial -3, no -1.

Medical history relevant to obesity: mild or borderline hypertension -4, gall bladder disease -3, musculo-skeletal problems -3, respiratory difficulties -2, hyperuricemia -4, abnormal glucose tolerance -2, skin abcesses -2, phlebitis -1, menstrual irregularity -1, Cushing's syndrome -1.

Improvement of health problems after successful weight loss: great improvement -1, some improvement -5, no change-2. Specific improvements appreciated by patients included respiratory status, agility and mobility, and back pain.

HOPES AND OPINIONS.

Future treatment plans or expectations: fast -4, psychiatric counseling -3, diet -4, exercise -1, surgical bypass -1. As one patient put it: "There is always the fear of putting it back on."

Hopes for future: reduce to specific weight (235,210,235,) 140 pounds, or 85, 35, 35, and 0 pounds overweight respectively) -4, successfully reduce without specific goal -4. One patient responded: "when people will say 'You look good.'"

Best possible treatment for obesity: fasting -2, fasting and diet -2, fasting plus psychiatric counseling and diet -2, individualized diet -2, ? surgical bypass -1.

Understanding of surgical bypass for obesity: effective but risky -2, too drastic to be used -4, questionable effectiveness but risky -2.

Source of knowledge about surgical bypass: physician(s)-4, literature and friends -4.

DISCUSSION

As has been decumented before, fasting is a highly effective method for rapid weight reduction (203, 205, 206, 207,13). The average weight loss of 43.4 pounds for these thirteen patients is considered successful by the criteria of 20 or 40 pound loss or Feinstein's reduction index, for which he defined as successful a value of 60 or above (102). However, these criteria of success were developed before fasting emerged as an acceptable method for weight reduction in the severely obese and probably tend to overestimate the success of a fast. Fasts were generally terminated for these patients when the incidental metabolic studies were complete and, although an average reduction index of 63 was achieved, most patients were still considerably overweight and in serious need of further large weight loss. The goal of fasting is called into question here. The initial reported series of fasts were of short duration, generally 2 weeks or less. Well tolerated, these fasts were viewed as beneficial not because of the magnitude of weight lost, but because they represented to patients a gratifying and successful running start on weight reduction and control (203, 207). Later reports indicated that longer fasts could be well-tolerated with losses greater than 100 pounds (206, 207). Admittedly, the risks of malnutrition and metabolic derangements are increased by longer fasts, and Bray had advised that fasts longer than two months are usually unwise (13).

Daily fasting weight loss was proportional to initial weight ($r=+0.64$, $p<0.05$), as has been reported elsewhere (207). An inverse correlation existed between average daily loss and length of fast ($r=-0.62$, $p<0.02$). Fluid losses early in the fast contribute to the greater weight loss seen earlier in the fast (205). Reports from the literature average about 2.5 pounds per day lost for short fasts (1 to 2 weeks), and closer to 1 pound per day for longer fasts (203, 205-207, 209, 210). The average loss per day for this series of 1.27 pounds over an average 34.6 days (5 weeks) compares well with that reported in other series. That the fast was well tolerated and compliance generally good for these patients also is in agreement with previous reports. 4 of 8 patients did describe the fast as emotionally difficult, and for one of these the fasting period was "one of the most difficult experiences of my life.". The need for screening out certain patients and/or strong psychiatric support during the fast is evident. Another patient commented that "psychiatry should be part of the program.". Innovation and change in the treatment setting and program could improve the quality of the fasting experience by specifically alleviating the stresses caused by boredom and confinement, and coping with very ill or non-fasting patients on the ward. Physical complaints were remarkably few, as the common side effects of orthostatic hypotension and electrolyte imbalances were well controlled medically. Hunger was a continued problem for only 1

of 8 patients, consistent with other reports. The hunger lack theory during fasting has been challenged, though (211). The uncertainty of the issue may be the result of the obese patient's difficulty in discerning physiologic cues relevant to his hunger and appetite control (88, 90). Indeed, it has been suggested that the obese are physiologically always hungry (12).

The duration of follow-up for these patients (mean = 7.1 months) is probably too short to consider as long-term. Bloom's original report followed-up his patients 2 to 9 months, finding that all maintained some of the fasted loss, and most maintained most of it (203). Hunscher's large follow-up study which included only 50% of the original patients - the others being lost to follow-up - found only one-third of the responders gained weight since hospitalization (208). However, a total of two-thirds of the entire group may have gained if one considers those lost to follow-up as failures. Harrison's follow-up report found 40% of his 62 patients had lost weight 1 year post-fast, and 24% showed loss after 2 years (209). McCuish's study was most discouraging, finding all his patients had gained weight after an average of 14 months of follow-up (210). In the present study, follow-up data was current for 7 of 13 patients, percentage quite consistent with Hunscher's experience. However, retrospective follow-up data was available for 12 patients. 4/12 regained all their lost weight, 2/12 regained some, and

6/12 lost weight since hospitalization. Again, this is remarkably similar to Hunscher's results. It was noted that the patients in this present study, like Harrison's and Hunscher's patients, tended to fare poorer as follow-up duration increased. Weight change correlated with follow-up results to appear less successful as the duration of follow-up increases. While only 2 of 8 patients felt their eating habits had been significantly changed since fasting, only 3 out of 8 felt that the fast had no effect at all on their eating habits. Bloom and Drenick reported that their patients felt that they had benefitted in terms of improved eating habits (203). Only 4/8 of the present group of patients have been able to successfully use a diet after their fast. 6/8, though, were generally satisfied with fasting as a treatment method. Although most realized that fasting did not get to the root of their problem, they were still gratified by their experience with a method with which they were able to lose a considerable amount of weight. The usefulness of fasting in a long term weight reduction and control program for severely obese patients as evidenced by this study's population remains limited. A few patients seem to have benefitted significantly, whereas they had not been successful with more conservative methods previously. Several patients, it would seem, did not benefit at all from the fast. Factors which influence success may be hypothesized based upon interview data, but the population studied is far too small from which to draw any conclusions.

A number of interesting patterns emerged from the interview data. These patients, with long and often life-time histories of obesity, coming from homes with obese parents, showed considerable insight into their condition. 7/8 could identify emotional stress as a major precipitant for weight gain. 4/8 have had experience with psychiatric counseling. Patients were also well aware of the role that eating habits play in their obesity. All 8 could admit that their food intake was large and snacking excessive. Nevertheless, their frustration was evident. One patient, who states that "insight helps," sadly admitted: "I'm addicted to food," and "I love food more than I love myself." Another disclosed, "I hate myself when I'm eating." What becomes clear is that what most of these very obese patients require is not so much advice, moralizing, or education about the basics of diet, but rather, support, understanding, and professional counseling.

The patients were also aware of many of the consequences of their obesity. Most striking to them was the public ostracism. "People don't understand obesity," one patient stated. Another admitted that he felt a closeness to fat people, and that they were all going through the same thing. Another felt that there is little variation in obese people. The potential value of group discussion for these patients is evident. Most patients were also aware that their obesity had affected their character and emotions. Only one patient denied any effects

of obesity to his psychosocial well-being. Health effects were also noted. Half of these patients sought fasting because of physical problems or fears. However, many of the effects were of the nature of chronic disease risk factors as opposed to present symptomatic difficulties.

Unfortunately, only one patient felt great improvement of his problems as a result of experiencing weight reduction. However, most felt some improvement and would probably benefit more if more excess weight were lost. Most patients found the weight loss achieved through fasting as gratifying in a variety of ways.

All these patients had a history of failure with other weight reduction methods. Diet and amphetamines stand out as the most frequently used unsuccessful methods. Two patients had had previous fasts and then regained the weight. Several patients had tried methods that have no sound basis for the treatment of obesity. It is noteworthy that 6 out of 8 patients felt the fast was the best treatment they had experienced, but that 4 of 8 patients also mentioned the fast as the worst treatment experienced. The success of the weight loss was undoubtedly gratifying for these patients, while the awareness that fasting may not be worthwhile in the long run also is present. Frustration is reflected in the responses to the fantasy question: "What would be the ideal way to lose weight, if it were possible?". Three patients were able to fantasize an energy burning pill, not too unlike the now

prohibited agent dinitrophenol (143). Three others were unable to imagine any ideal treatment. Concerning the surgical bypass, 6/8 had negative attitudes. Physicians, particularly non-surgeons, often have strong prejudices against risky surgical procedures. Evidence strongly favors that surgical bypass can be used effectively in properly selected massively obese patients (13, 227-232, 239). To pass on a contrary opinion to patients is not fair, as it would be equally inappropriate to lead a patient to believe that such surgery is without considerable risks and side effects.

All patients expressed hope to be able to reduce. Some set specific goals which were to a variable degree above their maximum ideal weight. 4/8 expected to fast again if need be in the future, 4/8 expected to rely on diet, and 3/8 mentioned the use of psychiatric counseling.

The information gathered through the interviews, while not sufficient in this small group to draw significant specific conclusions, does tell us a great deal about the very obese patient. He is generally an individual who has lived with obesity, treatments, and consequences for a long time, and has some insight into and considerable awareness of the behavioral aspects and consequences of his obese state. Despite all his experience, he is frustrated by the elusiveness of success. Several themes emerged that are relevant to specific treatment

methods:

1 - Many of these patients are excellent candidates for psychiatric counseling. They come motivated and with a modicum of insight into their problem.

2 - Many of these patients are reasonable candidates for behavior modification. They are motivated and aware of their bad eating habits and its importance in obesity. Although the efficacy of behavior modification for patients this obese is still not sufficiently proven, Stunkard's study is promising (191), and a trial for these patients would seem worthwhile.

3 - Many of these patients could benefit from group therapy. The burdens of obesity are considerable, and the group process offers patients a unique support system that often cannot be reproduced by an individual therapist.

4 - For most of these patients fasting was generally a gratifying experience. While they tend to desire refasting to achieve a rapid weight loss, they also realize that the fast alone often does little to insure long-term successful weight control. If recurrence occurs, or another major weight loss is needed, outpatient semistarvation as described by Genuth (218) is a promising and relatively safe method that could be worthwhile for these patients.

Data about the fast and follow-up tend to support that which has emerged as a consensus from the medical literature: Fasting is effective for rapid weight reduction and is well

tolerated with side effects and metabolic derangements well controllable. While most patients will not do well in terms of long-term weight control, some seem to benefit considerably whereas previous conservative methods had failed. Fasting has an appropriate place in the spectrum of treatment for the extremely or massively obese patient. It ordinarily ought to be utilized after less radical methods have been given a fair trial and proven ineffective, and usually in conjunction with professional counseling or supportive therapy to maximize success. If fasting proves ineffective in controlling massive obesity, alternative methods need be considered, including surgical bypass. A thorough understanding of an obese patient's weight history and experience, insights, feelings, and opinions about obesity and treatment can contribute to the planning of an appropriate and effective weight control program.

APPENDIX

I. OUTLINE OF INTERVIEW

I. Introduction - greeting and explanation of project
II. History
  A. General medical
  B. Obesity
    1. family: "Have other members of your family been overweight?"
    2. onset and precipitating factors: "When do you first recall becoming overweight? Can you recall things that happened in your life that preceded or somehow caused you to eat more or gain weight?"
    3. course - weight chronological history
    4. Treatments - successes, failures, opinions: "What method for losing weight has been best for you?... Why? Which methods didn't work?...Why? What would be an ideal way to be able to lose weight if it were possible?"
    5. consequences
      a. social: "Do you think being heavy has effected your social life?...How?...Any different after weight loss?"
      b. psychological: "Has being overweight effected your personality?...Your feelings?...Your mood?...Your behavior? Any different after weight loss?"
      c. medical: "How has being heavy effected your health? Any change after weight loss?"
    6. eating habits
      a. Meals - #, quantity, time, dieting, snacks
      b. foods - preferences
      c. insights: "Do you think eating habits are important in maintaining or changing weight? Are your eating habits conducive to maintaining or losing weight?...Why (not)?"
    7. excercise - amount, frequency, pleasure derived
III. Fasting experience
  A. Motives and expectations: "Why did you accept this treatment? What were your hopes and expectations of its success?...Any Fears?"
  B. Feelings, opinions about fasting experience: "How did you feel about fasting once you had started? ...Like or dislike?...What and why?...Any hunger?"
  C. Results - short and long term
    1. post treatment course --- present: weight
    2. eating habits, diet adherence: "Any change in eating habits? Are you using a diet?...Which? ...Stick to it?"
    3. medical follow-up: "Have you been seeing a doctor about your weight or health since you left the hospital?...How often?...What does he do or tell you?"

IV. "Prognostics"
- A. General satisfaction with fast as treatment; "Are you satisfied with fasting as a method by which you can lose or control your weight?"
- B. Plans for future treatment:"Do you expect to undergo a weight reducing regimen again? Which Method?...Why?"
- C. Hopes
  1. Weight problem - the future?: "Do you think weight will be a problem for you in the future? Why?"
  2. Best treatment: "In your opinion, what is the best treatment for overweight, including diet, exercise, medicine (pills), surgery, or any other method?...Why?"
  3. "What do you think or know about surgery for controlling weight? How did you learn this?"

V. Closing
- A. Questions?
- B. Thanks and well wishes

II. Correlation between average daily weight loss and initial weight. Simple linear correlation was tested, using the formula for the Pearson product-moment, correlation coefficient, r, where*"

$$r = \frac{\Sigma xy - \frac{(\Sigma x)(\Sigma y)}{n}}{\sqrt{(\Sigma x^2 - \frac{(\Sigma x)^2}{n})\ (\Sigma y^2 - \frac{(\Sigma y)^2}{n})}}$$

where: x = average daily weight loss
y = initial weight
n = fasted patients

Probability was tested for a t value, where:

$$t = r\sqrt{\frac{(n-2)}{(1-r^2)}}$$

III. Correlation between average daily weight loss and number of days fasted.

r coefficient calculated as above, where:
x = average daily weight loss
y = number of days fasted
n = fasted patients
t and probability calculated as above.

IV. Correlation between duration of follow-up and weight change since hospitalization.

r coefficient calculated as above, where:
x = duration of follow-up in months
y = change of weight in pounds since hospitalization
n = fasted patients with follow-up history

*Formula from J. Ipsen, P. Feigl: Bancrofts Introduction to Biostatistics, New York, Harper, 1970.

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